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SOLU-BILOPTIN (SH 550) AS A CONTRAST MEDIUM FOR PERORAL CHOLEGRAPHY

by

GEORG-FREDRIK SALTZMAN

The bile ducts are occasionally visible at the 12-hour examination during cholecystography with tri-iodized contrast media — preparations which were first introduced in 1949. If films are obtained 2 to 6 hours after the ingestion of the contrast medium the possibility of demonstrating the bile ducts is increased; the greater part of the medium passes through the ducts during this period on its way from the liver to either the intestine or the gallbladder. Although routine examinations of the bile ducts became possible in 1952 through the introduction of intravenous cholegraphy with Biligrafin, interest in the possibility of investigating the ducts with an oral contrast medium has not declined, and it is now possible to perform peroral cholegraphies as well. Various media have been tried for the purpose, and the best results hitherto reported have been obtained with Bilijodon-Natrium (Leo) in gelatine capsules, first introduced by GUNNARSON in 1958. Experiences with this contrast medium have also been described by SALTZMAN and by VIRTAMA.

Schering A.G. have for some time been working on the problem of producing a contrast medium for oral use in cholegraphy which would reduce the side-effects occurring with most of the earlier oral media and improve the possibilities of investigating the bile ducts. During the summer of 1959 the firm was able to place the first new preparation on the market. This was

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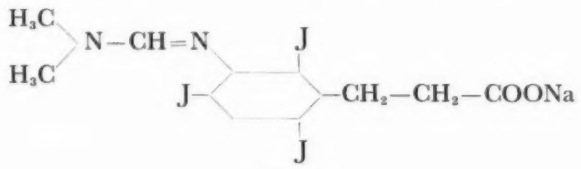
named Biloptin (experimental designation SH 514); it is the sodium salt of β-(3-dimethylamino-methylenamino-2,4,6-tri-iodophenyl)-propionic acid, with the empirical formula $(C_{12}H_{12}N_2O_2J_3)Na$; the iodine content is 61.4 %. The structural formula is given below. The preparation is supplied in capsules. Animal experiments with Biloptin have been carried out by HARWART et coll.



Biloptin

Preliminary reports on investigations with Biloptin in man indicate that from the standpoint of diagnosis the preparation is fully comparable to the best of the contrast media previously used for cholecystography (BOGATZKI, CRECELIUS, GOERKE, KEINER, MÜLLER und SIELAFF, WHITESIDE). The side-effects are stated by most of these investigators to be much less severe than those produced by other preparations for cholecystography; exceptionally, WHITESIDE reported nausea, vomiting, mild diarrhoea, and headache in more than a half of all cases, and in one case urticaria was also observed. My own experience of Biloptin is confined to 45 cholecystographies carried out in the conventional manner with administration of the contrast medium 12 hours before the actual examination. The concentration of the medium was not only good but fully comparable to that obtained with the best of the earlier media. Not a single one of my patients reported the slightest sensation of nausea; nor was there any diarrhoea. In view of these observations, WHITESIDE's experience is surprising. The only difference between his cases and mine was the size of the contrast dose. WHITESIDE gave his cases 6 gram, either in one dose or in two equal doses at 12-hour intervals. My cases received one dose of 3 gram. It is not unlikely that the numerous side-effects in WHITESIDE's material were due to the large dose, especially since nearly all the reactions in the cases given two doses of the medium occurred after the second dose. Obviously, a dose of 3 gram is large enough to produce satisfactory contrast density in the gall-bladder.

The previously mentioned papers show considerable divergence of opinion regarding the possibility of obtaining with Biloptin a contrast filling of the bile ducts sufficient for diagnostic purposes. The reason for this is probably that the examination technique was not in all cases directed primarily towards the demonstration of the bile ducts in the roentgen films. The best results were reported by BOGATZKI, who obtained a diagnostically satisfactory density in

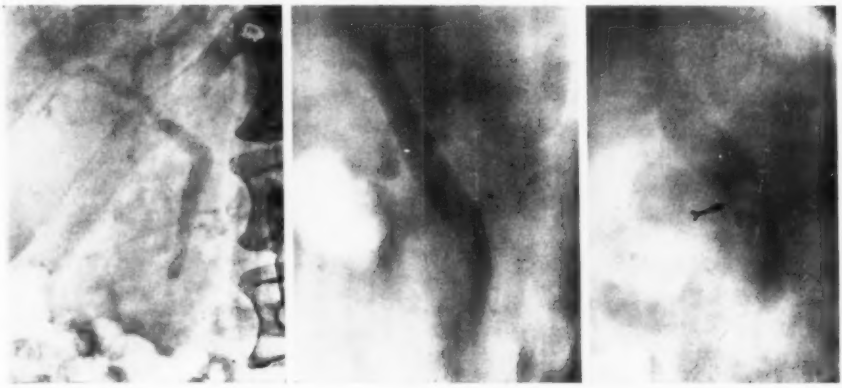


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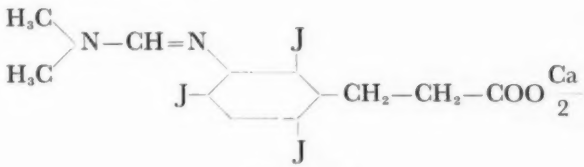
Fig. 1. Peroral cholegraphy with Solu-Biloptin. a) Narrow ducts. b) Wide common duct without concretions. c) Wide common duct with large stone (arrow).

the bile ducts in 65 per cent of his cases by using a fractionated method in which the patient received two doses, each of 3 g Biloptin at 12-hour intervals.

The writer has not studied Biloptin as a medium for examinations of the bile ducts. At the time when this preparation was first placed on the market trials were being made, through the courtesy of Schering A.G., with a similar medium for cholegraphy. This was known at first as SH 550, and is now sold under the name of Solu-Biloptin. As it had proved in animal experiments to be absorbed more rapidly than Biloptin it was considered to present better possibilities for producing high contrast density in the bile ducts. Solu-Biloptin is the calcium salt of β-(3-dimethylamino-methylenamino-2,4,6-tri-iodophenyl)-propionic acid, with the empirical formula $(C_{12}H_{12}N_2O_2J_3)_2Ca$. Its structural formula is given below:



Solu-Biloptin

The iodine content is 61.7 %. As this preparation has a much more agreeable taste than Biloptin it does not need to be taken in capsules. It is supplied in bottles containing 3 gram of the contrast medium in powder form, which

should be mixed with water before use. The brief reports that have appeared in the literature (KEINER, BOGATZKI, GOERKE) give no clear indication of the value of the preparation. BOGATZKI, in a material of apparently small size and not specified in detail, considered, however, that his results, from the standpoint of filling of the bile ducts, were comparable to those obtained by GUNNARSON with Bilijodon-Natrium.

In all our examinations, views were first taken 30 minutes after the administration of the contrast medium, and then at 15-minute intervals. As soon as the medium became visible in the bile ducts the patients were given 1 mg of morphine per 10 kg bodyweight. After optimal contrast density had been reached in the ducts a tomographic examination was carried out and the sphincter spasm was arrested with nitroglycerine or secergan.

The investigations were initiated with 8 examinations in which the patients received 3 g Solu-Biloptin. Only one patient found the taste of the contrast medium unpleasant. One patient experienced slight nausea; the other 7 had no side-reactions.

A diagnostically adequate contrast filling of the bile ducts was achieved in only 4 of these 8 cases, and even in those 4 cases the density was assessed as 'fairly thin'. Intravenous cholegraphy with Biligrafin was carried out in 2 of the cases in which no satisfactory concentration of the medium had been obtained and in both of them Biligrafin produced a high degree of density in the ducts.

Optimal contrast filling of the bile ducts was achieved in these cases 1 3/4 to 2 1/2 hours after the administration of the contrast medium. The gallbladder also filled rapidly. In the 5 cases in which the gallbladder had not been removed a high concentration of the medium was obtained after 3 hours; cholecystography with Bilijodon-Natrium had previously been performed in 4 of these 5 cases. The contrast density in the gallbladder was of equal degree with both these contrast media in 3 cases, and in 1 case a much higher density was obtained with Solu-Biloptin. Even these few cases indicate that a dose of 3 gram of the contrast medium is probably sufficient to permit an examination of the gallbladder. In the hope of improving the conditions for studying the bile ducts we soon began to give the patients a double dose, i. e. 6 g Solu-Biloptin.

Up to now we have undertaken 62 cholegraphies in 61 patients, using 6 g Solu-Biloptin. The powdered contrast medium was mixed with 1 to 2 glasses of ordinary tap water and all patients swallowed the whole of this dose without difficulty. Eleven of the patients found the taste of the medium unpleasant, while the others were indifferent to it, and one even considered it was nice.

Not even with this fairly large dose of contrast medium were the reactions troublesome. Among the 61 patients, 14 experienced nausea after taking the medium, 10 of them stating that their sensations were 'slight'. Vomiting occurred in only one of these cases, but this patient had had repeated vomiting attacks the same day, before the examination was begun. No allergic reac-

a b c

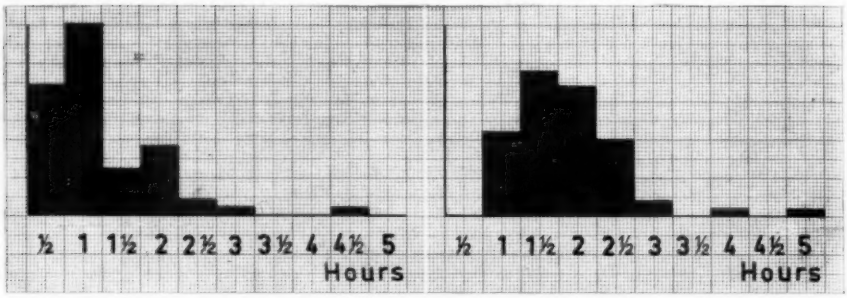
Fig. 2. Conventional roentgenogram (a) and tomograms (b and c) from peroral cholegraphy with Solu-Biloptin. The interference caused by contrast medium in the stomach and the duodenal bulb is almost completely eliminated by tomography.

tions were observed. The effect on the blood pressure and pulse rate has been described in another connection (SALTZMAN and SUNDSTRÖM). No blood pressure fall of the type produced by Biligrafin was recorded.

Diagnostically adequate contrast density in the bile ducts was obtained in 51 of the 62 examinations in which the patients had received 6 g Solu-Biloptin. In 6 cases, the ducts were not demonstrated distinctly enough for diagnosis, and in the remaining 5 cases they were not visible.

Closer analysis of the 5 cases in which the bile ducts failed to fill revealed that two of the patients had cirrhosis of the liver. In 2 other cases the intestine contained a large amount of unabsorbed contrast medium during the entire examination; in one of these cases another examination made with the same contrast medium one week later resulted in apparently complete absorption of the medium, and the bile ducts filled satisfactorily. The bilirubin content of the blood was between 0.7 and 1.4 mg % in these 5 cases. There was also a case of cirrhosis of the liver among the 6 cases in which the bile ducts filled, although not distinctly enough for diagnosis. In another of these cases, a large amount of unabsorbed contrast medium was observed in the intestine.

Intravenous cholegraphy with Biligrafin-forte was carried out later in 5 of the 11 cases in which peroral cholegraphy with Solu-Biloptin had not given satisfactory contrast density. The results of the two examinations were the same in one of these cases, i. e. no filling of the ducts was obtained with either medium.



a b

Fig. 3. a) Time between the administration of the medium and its first appearance in the bile ducts in present material. b) Time from the administration of the medium to its optimal concentration in the bile ducts. Every case corresponds to 2 mm on the mm-paper.

In the other 4 cases, Biligrafin-forte produced diagnostically adequate filling of the ducts. These 4 cases in which intravenous cholegraphy produced a better result than the oral form may perhaps give the impression that the intravenous method is superior to the peroral method with Solu-Biloptin. It should, however, be pointed out that two of these patients had had jaundice; in one of them the serum bilirubin content had dropped from 1.4 to 0.4 mg % between the peroral and intravenous cholegraphies. In the other case as well, the conditions favouring a satisfactory result may have been better at the intravenous cholegraphy, which was performed one week after the peroral examination. The bilirubin values are not available in this case. It might be mentioned in this connection that to perform cholegraphy in patients with serum bilirubin values of over 2 mg % appears in general to offer little hope of success. This limit seems to apply in both intravenous and peroral examinations. It should, however, always be borne in mind that a serum bilirubin value may drop rapidly and hence may already be out-of-date one day later.

It should also be remembered in making comparisons between the peroral and intravenous cholegraphic methods that GUNNARSON in a large material observed that while the intravenous method certainly does sometimes give better results than the oral technique the opposite is by no means uncommon. We have not had an opportunity to perform intravenous cholegraphy in cases in which the oral method has given a diagnostically satisfactory result.

It is, however, obvious that intravenous cholegraphy usually produces a higher concentration of contrast medium in the bile ducts than the peroral method in those cases in which the orally administered medium remains wholly or partially unabsorbed. This is an unusual occurrence, however. As already mentioned, there were only 3 cases in the present material in which any appreciable amount of unabsorbed contrast medium was observed in the intestine.

The long and variable interval between the administration of the contrast medium and optimal filling of the ducts (SALTZMAN) has previously formed one of the most troublesome disadvantages of the peroral method from the practical standpoint. Solu-Biloptin seems to reduce this difficulty considerably. In the 1 examinations in which the bile ducts were demonstrated, the first signs of contrast medium in the ducts were usually noted 1/2 to 2 hours after the medium had been swallowed (Fig. 3a); in over one-half of all cases the ducts were already visible one hour after administration. In exceptional cases, 3 to 4 1/2 hours elapsed before the first signs of filling appeared.

Optimal contrast density in the ducts was reached in the majority of the cases within 2 1/2 hours (Fig. 3b). Only in a few cases was the interval longer; in one case it was as long as 5 hours. With all forms of oral cholegraphy used up to now — and the Solu-Biloptin method is no exception — the bile ducts may be partially concealed by contrast medium in the pyloric portion of the stomach and in the duodenal bulb. This interference can be readily eliminated with the aid of tomography (Fig. 2). We are definitely of the opinion that tomography forms an invaluable complement to both intravenous and peroral cholegraphy.

The excretion of contrast medium through the kidneys sometimes causes difficulties in the interpretation of the bile ducts in intravenous cholegraphy, especially if an overdose of the medium has been given. For β-(3-dimethylaminomethylenamino-2,4,6-tri-iodophenyl)-propionic acid and its salts, the proportion between the bile and the urine excretion varies in different mammals (HARWART et coll.). With a dose of 3 gram in adults, approximately one-half of the amount seems to leave the body through the one channel and one-half through the other channel. The excretion with the urine apparently takes place so slowly, however, that contrast filling of the renal pelves is not often seen. Visible filling of the renal pelves was noted in only 2 of our examinations and not even in these cases was any difficulty experienced in the assessment of the bile ducts.

The gallbladder was distinctly demonstrated in the films in those cases in which it was still in position. A tendency to layer formation between contrast-bearing and non-contrast-bearing bile was observed in a few instances but this was not so marked as with Biligrafin. The slight difficulties associated with such layer formation can be readily overcome by taking further views with a horizontal beam after a fatty meal; this usually results in a homogeneous mixture of bile and contrast medium.

Conclusions

Our investigations have shown that it is possible to demonstrate the bile ducts just as effectively by means of Solu-Biloptin as by intravenously injected Biligrafin-forte or orally administered Bilijodon-Natrium.

As an oral contrast medium for cholegraphy, Solu-Biloptin has proved to be definitely superior to Bilijodon-Natrium. The examination is less trying for the patient, and the transport to the site of absorption in the small intestine takes place at a much faster rate; hence the examination can be carried through more rapidly and it is easier to reserve adequate time for it. Another advantage is that Solu-Biloptin does not need to be taken in capsules. Most patients can drink a water suspension without difficulty, whereas there is a small group of patients, about 2 to 4 % in our experience, which cannot be persuaded to swallow capsules.

Many investigators may perhaps wonder whether peroral cholegraphy has any mission to fill, seeing that, diagnostically speaking, intravenous cholegraphy with Biligrafin is a fully satisfactory method for the examination of the bile ducts. Although Solu-Biloptin has considerably reduced the examination time for peroral cholegraphy, intravenous cholegraphy can usually be carried out more rapidly.

The two methods appear to complement each other. Cases are encountered in which peroral cholegraphy is to be preferred to the intravenous method. Biligrafin causes a number of side-reactions, and deaths have been reported (FROMMHOLD & BRABAND). In the dose commonly employed, Biligrafin-forte usually causes a fall in blood pressure (SALTZMAN & SUNDSTRÖM); this fall is probably of little practical significance in young persons with a sound heart but it may be dangerous in patients with arteriosclerosis or cardiac insufficiency. In all probability, the majority of the deaths have been a result of the fall in blood pressure. We have not encountered a single case with a definite blood pressure drop in connection with peroral cholegraphy. Patients who react positively to a Biligrafin test appear to constitute another group that should be examined by the oral method. A peroral examination is more suitable for an investigation of both gallbladder and bile ducts than one using Biligrafin, since the latter contrast medium seems to cause interfering layer formation between contrast-bearing and non-contrast-bearing bile more often than the oral media. Such an examination does not, however, imply any saving in time for the roentgen department as compared with a combination of conventional cholecystography and intravenous cholegraphy.

To summarize it may be said that Solu-Biloptin has improved the possibilities for examining the bile ducts with oral media. Its rapid transport to the site of absorption in the small intestine constitutes the most notable advantage offered by this preparation over other comparable contrast media. An examination with Solu-Biloptin takes longer to perform, however, than intravenous cholegraphy with Biligrafin. It must therefore be admitted that Biligrafin still holds its position as our most important contrast medium for cholegraphy. We consider, however, that peroral cholegraphy is preferable in the aged, in patients with cardiovascular diseases, and in those who show a positive reaction to a Biligrafin test.

SUMMARY

A new contrast medium for investigation of the bile ducts, Solu-Biloptin, has been tried ut, and comparisons are made with other media. The use of intravenous and peroral cholegraphy as complementary examinations is considered advisable, and the indications for the wo methods are discussed.

ZUSAMMENFASSUNG

Ein neues Kontrastmittel, Solu-Biloptin, wurde zur Untersuchung der Gallenwege geprüft und wird mit anderen Kontrastmitteln verglichen. Die intravenöse und perorale Cholegraphie werden als sich ergänzende Untersuchungen empfohlen und die Indikationen für beide Methoden besprochen.

RÉSUMÉ

L'auteur a expérimenté un nouveau moyen de contraste pour l'examen des voies biliaires et l'a comparé à d'autres moyens de contraste. Il pense que l'utilisation de la cholégraphie par voie intraveineuse et de la cholégraphie par voie orale comme méthodes complémentaires est à conseiller, et il étudie les indications de ces deux méthodes.

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CHONDROSARCOMA OF THE BONES OF THE HAND

Report of 3 cases

by

ELMAR JAKOBSON and HARLAN J. SPJUT

Benign cartilaginous tumors, or enchondromas, of the bones of the hands are not infrequently encountered but only rarely (9 reported cases) does a chondrosarcoma arise primarily in these situations (DAHLIN et coll. 1958, JAFFE 1958, LICHTENSTEIN 1959, LANSCHE et coll. 1958). The essential data of the nine reported cases of chondrosarcoma of the hand were tabulated in the last paper.

We have studied three cases from the bone tumor registry of Karolinska Sjukhuset. One of these was a chondrosarcoma of an index finger, the second a chondrosarcoma of a third metacarpal and the third case a chondrosarcoma of the fifth metacarpal bone. An additional case of a chondrosarcoma of a metacarpal, without clinical data, has appeared in the literature (EIDE et coll. 1958). There are thus to our knowledge, counting our three cases and those from the literature, 13 known cases of chondrosarcoma of the bones of the hand.

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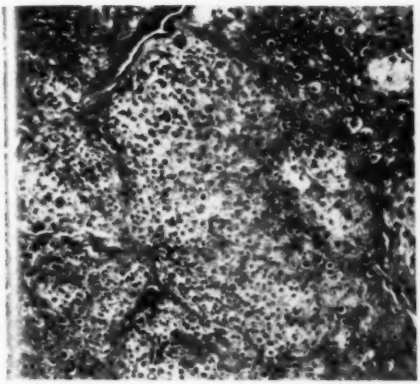

Fig. 1. Case 1. First local resection, May 1936. The chondrosarcoma retains a lobular pattern; many bizarre nuclei present. H. and e. × 80.

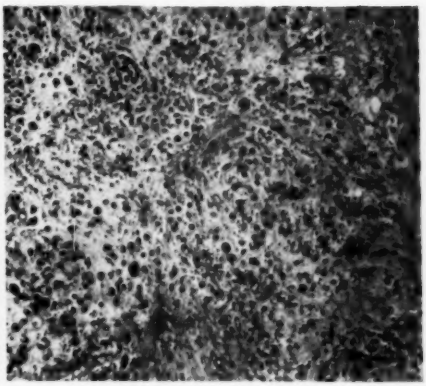

Fig. 2. Amputation specimen October 1936, of chondrosarcoma in fig. 1. Histologically similar to fig. 1. H. and e. × 80.

Case reports

Case 1. A woman, aged 56, had for two years noticed a swelling of her right hand which arose at the base of the right index finger and gradually involved the palm and increased to the size of a small egg. Examination revealed a 'bow-shaped' mass that extended from the base of the index finger to the area between the thenar and hypothenar eminences. Local excision was performed in May 1936. The tumor which proved to be a chondrosarcoma was described as lobated, the size of a thumb, and firmly attached to the third metacarpal. Irradiation therapy (1 600 r) was given to the tumor area in June 1936. Recurrence was evident in October 1936 and amputation of the first three fingers and the respective metacarpal bones was performed. The patient was symptom-free until May 1942 when a nodule 3 mm in diameter was noted in the operative scar of the hand; this was excised and proved to be a tumor similar to that of the metacarpal. The patient died in December 1954 at the age of 77 years of thrombosis of the superior mesenteric artery. No evidence of recurrence or metastases at necropsy. The period of survival after the first excision of the tumor was 18 years.

Pathology examination. The excised tumor measured approximately 2.5 × 1.5 cm in its greatest diameters. Its surface was lobulated and cartilaginous and the mass was firmly attached to the metacarpal. Microscopically the tumor was irregularly lobulated with foci of hyalinization; the hyaline cartilage cells were poorly differentiated with many bizarre cell shapes and nuclei (Figs 1 and 2). A rare mitotic figure was noted. Sections from the recurrent tumors in 1936 and 1942 showed similar structures as in the primary tumor. The nodule noted in 1942 was surrounded by fibrous tissue and in all likelihood represented an implant growth as a result of the previous operative procedures.

Case 2. Woman, aged 52, who, in 1940 (one year before admission) noted a hard, slowly progressing, bony swelling on the front of the left index finger. On examination the volar surface of the middle phalanx of the index finger was swollen, firm, and resilient, with the consistency of hard cartilage.

Roentgen examination. An expansion of the middle phalanx of the index finger with destruction of the cortex was evident. The distal joint appeared to be partly destroyed. Irregular material was seen in the soft tissue; they were probably fragments of bone as they did not have characteristics of calcium deposits so often present in chondrosarcoma. Within the medullary space clear areas caused by the tumor together with what appeared to be a bursting out of the growth into the soft tissues suggested that the lesion had arisen centrally, perhaps as an enchondroma (Fig. 3). Amputation, without prior biopsy, of the left index finger was carried out in March 1941, and produced good results with no recurrence. The patient died in June 1954 from renal insufficiency. No evidence of recurrence or secondaries.

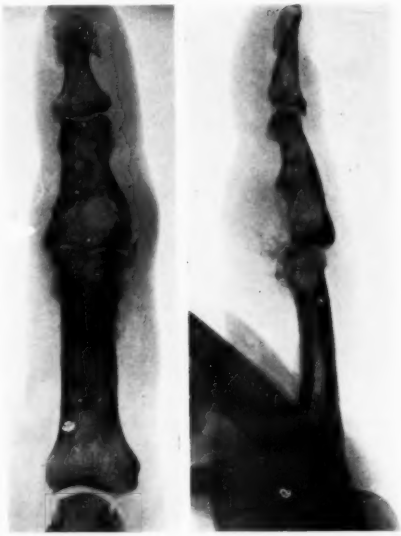

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Fig. 3. Case 2. a) P. a. Translucent expanding lesion of the middle phalanx. b) Lateral. The tumor is seen to extend into the soft tissues.

Pathology examination. A sagittal section through the phalanx showed a cartilaginous mass involving the proximal half of the bone. At one point the tumor had destroyed the cortex and extended into the surrounding soft tissue to within 3 mm of the skin anteriorly. There was no obvious involvement of the interphalangeal joint. Microscopically the tumor was irregularly lobulated and composed of cartilage, the cells and nuclei of which varied greatly in size. At the periphery of the tumor, immature chondrocytes were seen and many binucleate and a few trinucleate cells noted. A number of cells had large bizarre nuclei; no mitoses were present. The cortical bone was eroded and destroyed in one area (Fig. 4). The tumor penetrated the joint cartilage at one point (Fig. 5); no residual enchondromatous cartilage was obvious.

Case 3. Woman, aged 58, was admitted in December 1956 because of a swelling of the left hand. Trauma some thirty years previously had produced a small nodule on the lateral aspect of the hand. This had gradually increased in size until it interfered with the patient's daily chores but produced a feeling only of pressure. Examination showed a hard mass about the size of a tangerine, firmly fixed to the fifth metacarpal of the left hand. The fourth metacarpal appeared also to be involved.

Roentgen examination. Most of the distal two-thirds of the fifth metacarpal bone including the distal joint surface were destroyed (Fig. 6). The neoplasm was expansile and sharply circumscribed in the soft tissues, except at its proximal margin. The speckled calcification which was present was suggestive of a cartilaginous tumor although such deposits are characteristically larger and have a granular appearance; residual bone may have accounted for at least some of the opacities noted. Amputation of the left fifth finger and metacarpal was performed in December 1956. The patient has remained well and without signs or symptoms up to March 1960 (over 3 years after operation).

Pathology examinations. The tumor measured 4 cm in diameter and appeared to be encapsulated and nodular. The cut surfaces were gelatinous, grey, friable, partly calcified and

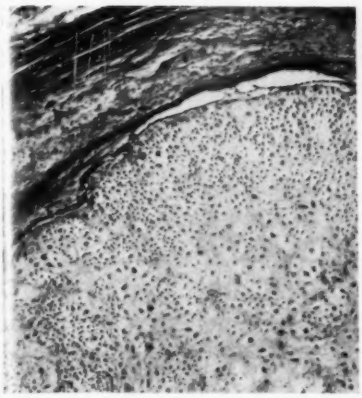

Fig. 4. Part of chondrosarcoma (Case 2) has grown beyond the cortex into soft tissues. Many bizarre, large and plump nuclei. H. and e. × 80.

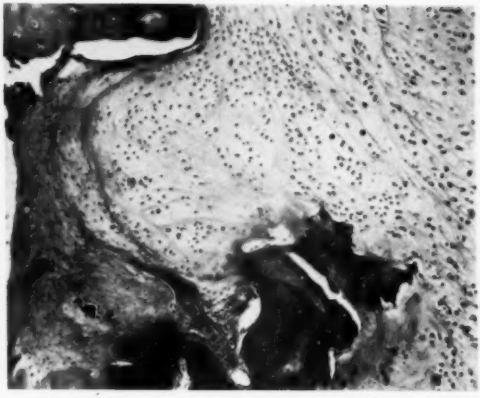

Fig. 5. (Same case as in figs 3 and 4.) Photomicrograph showing the tumor invading the cartilage of the proximal joint surface. H. and e. × 80.

necrotic. The growth extended into and partly destroyed the metacarpophalangeal joint. Microscopy showed a lobulated, partly calcified, moderately well differentiated chondrosarcoma with some poorly differentiated areas (Figs 7 and 8). Numerous bizarre nuclei and occasional multinucleated cells were present; no mitotic figures evident. The tumor had destroyed the bone and extended into the surrounding soft tissues. Invasion of the metacarpophalangeal joint was confirmed histologically.

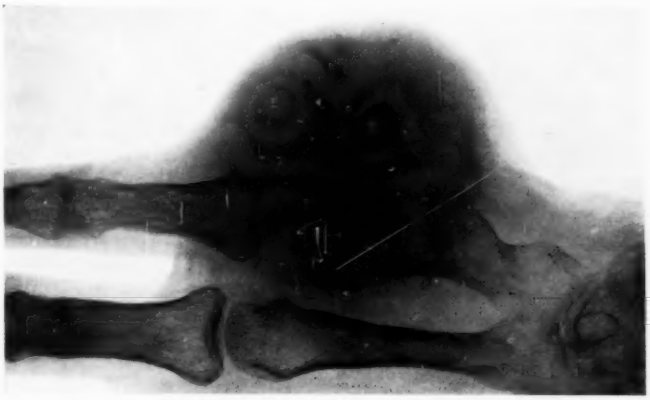

Fig. 6. Case 3. Expansile eroding tumor of M 5 with destruction of the distal joint surface. The other bones of the hand are intact.

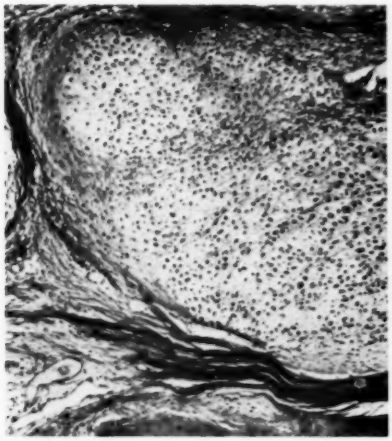

Fig. 7. Lobular pattern of tumor (Case 3) with richly cellular cartilage and bizarre nuclei of the cartilage cells. H. and e. × 70.

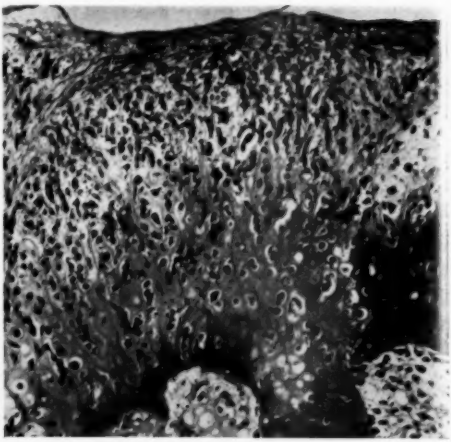

Fig. 8. Chondrosarcoma (Case 3) involving the distal joint of the metacarpal. (Joint surface and joint space at top.) H. and e. × 150.

Discussion

Of the cases of chondrosarcoma of the hand reported in the literature together with our three cases whose ages are known, only one of the 11 patients was less than 52 years of age, i. e. a man aged 38. The sex distribution of the patients of whom the sex is known is equal, being similar to that of enchondroma of the small bones (GESCHICKTER & COPELAND 1949) and of chondrosarcoma of other parts of the skeleton. The bones involved include a phalanx in 7 cases, a metacarpal in 5 cases and a carpal bone in 1 case.

None of our three patients developed evidence of recurrence or metastatic disease after follow-up periods of 13 years, 18 years and 39 months respectively. However, distant metastases (pulmonary and cutaneous) from chondrosarcoma of the hand bones have been reported (COLEY et coll. 1954, CRUICKSHANK 1945). Pulmonary metastases in one case appeared 25 months after therapy (CRUICKSHANK). The short follow-up period (only three known to have been controlled over 30 months) of most of the previously reported cases (LANSCHE et coll.) precludes any satisfactory conclusion as to the fate of patients having chondrosarcoma of the bones of the hand.

The histologic demarcation between enchondromas of bone and central chondrosarcomas is often ill-defined and seems to vary from examiner to examiner. In view of the fact that enchondromas of the bones of the hand are often quite cellular, especially in a young subject, some doubt may be raised as to the validity of a histologic diagnosis of chondrosarcoma. The

microscopic alterations are often subtle although the presence of plump nuclei, large nuclei, bizarre nuclei, and binucleate cells will usually point to the nature of the growth, and the diagnosis will be reinforced by recurrence of the tumor and invasion of the soft parts. All of the preceding histologic and gross features were present in Case 1, and all, except recurrence, in Cases 2 and 3. For arriving at a final diagnosis it is important to compare the clinical and roentgenographic findings.

Because of the location of the lesion it is not unreasonable to postulate that a chondrosarcoma has its origin in an enchondroma; the bones of the hand are a common site for the latter. The pathologic and roentgenographic data of our cases furnish no evidence, however, of any pre-existent enchondromas and in none of these cases were enchondromas found in other bones of the hand. The destruction of the bone and the joint, and the location and the calcification of the tumor of the fifth metacarpal as shown in the roentgenograms in these cases, might well have suggested a malignant cartilaginous tumor. That a chondrosarcoma may arise from an enchondroma, especially in cases of enchondromatosis and enchondromas of the long bones, is generally accepted. If a chondrosarcoma of the hand does arise from a pre-existing cartilaginous lesion, as one of the cases reported (LANSCHE et coll.) suggests the transformation from benign to malignant cartilage must be very slow. Enchondromas are most commonly diagnosed in the third and fourth decades of life (GESCHICKTER & COPELAND) whereas in the small group of chondrosarcomas of the hand the diagnosis has been made in the sixth and seventh decades, with the one exception mentioned.

It is difficult to evaluate the treatment of a chondrosarcoma of the bones of the hand since the follow-up period of most of the cases has been relatively short. Most of the cases, including ours, have been treated by amputation of the affected phalanx or part of the hand.

SUMMARY

Three cases of chondrosarcoma of the bones of the hand are reported, making a total of 13 known cases. The diagnosis, the course, and the treatment are considered.

ZUSAMMENFASSUNG

Drei Fälle mit Chondrosarkomen der Handknochen werden mitgeteilt. Hiermit erhöht sich die Gesamtzahl der bekannten Fälle auf 13. Die Diagnostik, der Verlauf und die Behandlung der Erkrankung werden besprochen.

RÉSUMÉ

Les auteurs présentent trois cas de chondrosarcome des os de la main, ce qui porte à 13 le total des cas connus. Ils décrivent le diagnostic, l'évolution et le traitement.

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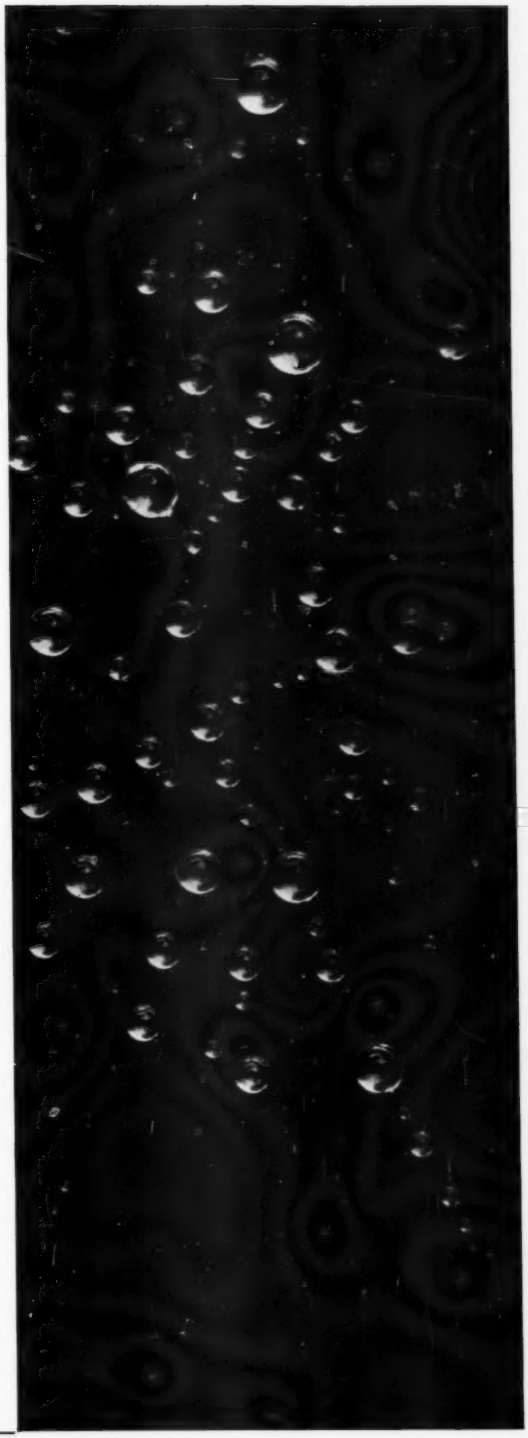

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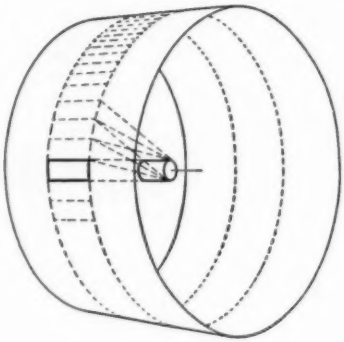

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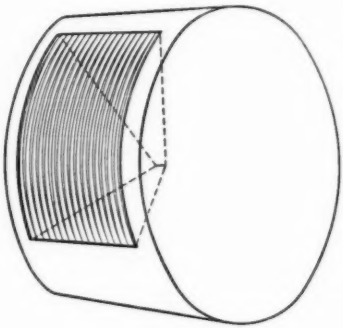

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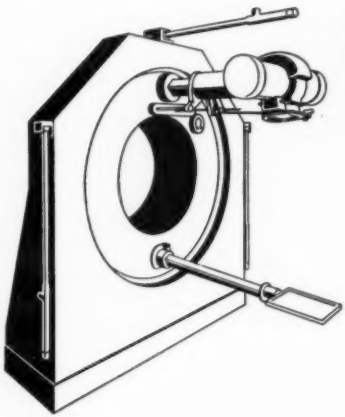

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CORRELATION OF UROGRAPHY AND TESTS OF RENAL FUNCTION

by

N. P. G. EDLING, C. A. EDVALL and C. G. HELANDER

In 1956 the present authors compared urography with inulin and PAH (para-aminohippuric acid) clearances of individual kidneys as a test of renal function in a series of normal cases and cases of renal disease. This further communication deals with the correlation of the urographic findings with the clearance and urinary concentration tests in a series of cases of hyperparathyroidism.

Material and Methods

The material consisted of 20 cases of hyperparathyroidism in which the blood calcium, initially elevated, reverted to normal levels after parathyroidectomy. Two of these had a single functioning kidney, one having had nephrectomy for calculi, and the other showing evidence of non-function of one kidney by urography and clearance tests.

A total of 43 urographies were performed, 10 before and 33 after parathyroidectomy. In 38 the contrast material was 40 ml Urografin (sodium + methyl-

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glucamine diatrizoate) 60 %, and, in the remaining 5, either 20 ml Urografin 60 % or 20 ml Miokon (sodium diprotrizoate) 50 %. The urographic density was estimated subjectively and considered as either normal or poor. All doubtful or borderline densities were relegated to the poor category.

The analytic methods of clearance determination were described by EDVALL (1958). Samples of urine were obtained by bladder catheterization. Normal clearance figures of both kidneys for inulin are 92 to 146 ml/min and for PAH 400 to 710 ml/min. In the current series clearances were measured in 12 cases both before and after parathyroidectomy, in 2 before, and in 6 after. A total of 39 inulin and PAH clearance determinations were performed.

The concentrating power of the kidneys was determined according to a modified concentration test in which the lower normal limit is a specific gravity of 1.025. In all but one case concentration tests were performed in the preoperative period and all cases had multiple tests after operation.

In his earlier study EDVALL found postoperatively generally diminished inulin clearances (glomerular filtration), and only in advanced cases was there a decrease in the PAH clearance (renal plasma flow). Although the change in the clearance figures was of statistical significance the departures were of lesser degree than those of the concentration tests (see below). In the present series initially normal clearances remained within normal limits and reduced clearances were unaltered postoperatively, except in 3 cases. Divided thus, 5 cases had normal clearances, 12 reduced clearances and 3 had a clearance of either inulin or PAH reduced pre- or postoperatively.

According to HELLSTRÖM (1959) the concentrating power of the kidneys in hyperparathyroidism is lowered, but improves in most cases after parathyroidectomy. The 19 cases in this series which were examined preoperatively all displayed reduced concentration power with the exception of one with a borderline value of 1.025.

The time interval between the urographies and clearances was in 13 cases 12 days or less and in the remaining 7 cases from 1 to 16 months (cf. legend to Fig. 1). In the latter, repeated clearances indicated stat onary conditions in the kidneys. This was furthermore the case with urographies or concentration tests when performed as routine follow-up examinations postoperatively. In addition, there was clinically no abrupt change or complication of the disease. Due to the chronic nature of the condition a comparative study of the different examinations seems reasonable even if the time interval in some cases is large.

Results

According to the density of the renal pelves at urography, 14 cases (average age 52.0 years) had good contrast medium excretion and in 6 (average age 51.8 years) it was poor. All urographies performed with 20 ml of contrast material produced a good density of the contrast medium in the pelves. In

Fig. 1. Hyperparathyroidism and nephrocalcinosis. One day before and about one and two weeks after parathyroidectomy the C_{IN} values were 47, 33, and 38 ml/min, and the C_{PAH} values 193, 149, and 144 ml/min respectively. The concentration power varied between 1.015 and 1.020 at tests carried out just before and repeatedly during 15 months following the operation. Urography (40 ml Urografin 60 %) about 15 months after the operation showed good density (only right kidney reproduced).

Fig. 2. Hyperparathyroidism and nephrolithiasis. Three days before and about a week after parathyroidectomy the C_{IN} values were 75 and 46 ml/min, and the C_{PAH} values 428 and 242 ml/min respectively. The concentration power improved from 1.022 to 1.027 in a period of about 9 months from operation. At repeated urographies (40 ml Urografin 60 %) good density was obtained (only left kidney reproduced).

no case was there any perceptible difference in the roentgenographic density between the pre- and post-parathyroidectomy examinations.

The 14 cases with good filling have been divided into 3 groups according to the clearance values. The first 5, including the two with single functioning kidneys, had normal clearances. In this group seven urographies were performed. The concentration power in one was always normal; it improved in 3 cases, in one to a normal level. Only postoperative examinations of concentration power were carried out in the remaining case in this group and showed a moderately reduced value. A further 3 cases (nine urographies) with good urographic density (Fig. 2) had either a reduced inulin or PAH clearance. In all three the concentration power improved to normal after operation. The remaining 6 cases (ten urographies) showing good density had both clearances reduced.

Fig. 3. Hyperparathyroidism and nephrolithiasis. Two days before and ten days after parathyroidectomy the C_{IN} values were 34 and 30 ml/min, and the C_{PAH} values 209 and 115 ml/min, respectively. The concentration power improved from 1.012 to 1.020. At two urographies (40 ml Urografin 60 %) poor density was obtained (only left kidney reproduced).

Two of these had a normal density only on one side, the pelvis and calyces of the other kidney being but faintly outlined due to obstruction by a calculus or to severe damage; their clearance measurements were reduced to less than half the normal value for two kidneys. Of the 4 cases with adequate contrast density bilaterally (Fig. 1) 3 had moderately decreased and one markedly decreased clearances. In this sub-group the concentration power improved in 4 cases (one to normal) and remained at the same reduced level in 2.

The 6 cases (17 urographies) with poor contrast density at urography (Fig. 3) had all clearances reduced. Three had moderately decreased and 3 markedly decreased clearances. The concentration power was always below normal, but showed some postoperative improvement in 4 of the 6 cases.

Discussion

In our previous paper (1956) on the same subject the physiology of the nephrons and the urographic technique were summarized. Essentially the same urographic technique was employed in this series and included preliminary dehydration and ureteral compression, features which tend to increase the concentration of contrast medium in the urine and the filling of the renal

elves respectively. It was found in the earlier study that good contrast density f the pelves does not always indicate normal functional capacity of the kidneys, nd conversely, that poor density does not always mean reduced capacity. welve out of 15 cases with reduced density had reduced clearances, but only out of 15 cases with urographic density considered normal had normal learances.

In the present material, concentration tests, as well as inulin and PAH learances, are used as functional tests for comparison with urographic density.

In the 14 cases showing good urographic density 5 had normal clearances nd 9 reduced value of one or both clearances. The concentration power was ormal in one case and initially low in 12 cases; of the latter, after operation 0 improved (5 of them to normal levels) and 2 remained unchanged; the emaining case was examined only postoperatively and showed low concentration.

Good filling of the renal pelves in urography is therefore possible despite the fact that the clearances and concentration tests may be low. This may seem inconsistent since the contrast medium concentration in the urine must depend, in addition to the dose of contrast material, upon both the tubular excretion and the tubular water reabsorption from the glomerular filtrate (concentrating power). EDVALL found, however, that in hyperparathyroidism the tubular water reabsorption mechanism is less severely and less permanently damaged than the tubular excretion and glomerular filtration. Furthermore it is known that the range of the tubular water reabsorption is much greater than that of the tubular excretion. There is in addition an enhancement of the contrast density due to the above-mentioned features of the urographic method, preliminary dehydration and strong ureteral compression which is applied some minutes after the injection and allows the initial pelvic content of low contrast content to flow away. All of these factors may contribute to the density of the renal pelves and compensate more or less for any deficit in renal function.

All of the 6 cases showing poor urographic density had reduced clearances and concentration power; in 4 the concentration power improved postoperatively but not to normal values and was unchanged in the other 2 cases. Thus, the urographies, clearances, and concentration tests in this group all correspond and satisfactorily reflect reduced renal capacity. The renal capacity when the urographic density becomes noticeably poor, is apparently so low that any intensification in the density produced by the urographic method is no longer able to mask the deficiency in renal function. It must, however, always be remembered that decreased urographic density may also result from extrarenal disease factors or from a less than optimal urographic technique.

The present results agree in general with those of our previous paper relative to comparative urography and renal function tests. The methods seem consistently to correspond where the urographic density is poor, but to be undependable in the presence of adequate urographic density.

SUMMARY

The relation between urography and inulin and PAH clearances and concentration test as an indication of the value of urography as a test of renal function were investigated in 2(cases. It appears that careful urographies producing poor contrast filling in young and middl aged patients not suffering from polyuria or circulatory failure suggest reduced renal capacity

ZUSAMMENFASSUNG

Die Relation zwischen Urographie, Inulin und PAH clearance und Konzentrationsversucl wurde in 20 Fällen untersucht, und hierbei der Wert der Urographie als Nierenfunktionstes geprüft. Es hat den Anschein, dass schwache Kontrastfüllung bei Patienten jugendliche und mittleren Alters, die nicht an Polyurie und Zirkulationskrankheiten leiden, eine herab gesetzte Nierenfunktion vermuten lässt, unter der Voraussetzung, dass die Urographie sorg fältig durchgeführt wurde.

RÉSUMÉ

Les auteurs ont étudié sur 20 cas la valeur de l'urographie comme test de la fonction rénale par comparaison avec les clearances à l'inuline et au PAH et avec les épreuves de concentration. Il en ressort que les urographies bien exécutées qui donnent un mauvais contraste chez des sujets jeunes et d'âge moyen, exempts de polyurie ou d'insuffisance circulatoire, doivent faire penser que la valeur fonctionnelle des reins est diminuée.

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INTRALUMINAL DUODENAL DIVERTICULUM

Report of a case

by

ROLF KÖHLER

An intraluminal diverticulum is a sac-like structure covered with mucosa on its outer and inner surfaces. I have found only three cases of this radiologically demonstrable, congenital anomaly in the literature, and to these I am now able to add a fourth case.

Case report

A woman, aged 33, had for the previous five years experienced pain in the epigastrium after meals. Three years previously she had had medical treatment for a gastric ulcer; relief of symptoms and healing occurred within six weeks. Some months later she again complained of epigastric pain immediately after meals; she also had nausea and wind, the latter for a period of about two and a half years. No symptoms between meals.

On admission, there was slight vague tenderness on deep palpation over the epigastrium. No free HCl in stomach. TA 16. Haemoglobin 12.7 g, SR 15 mm/hr. The stools were benzidine-negative.

Normal cholecystography. No obvious abnormality of the stomach. The duodenum was moderately dilated. An elongated accumulation of contrast medium was seen filling almost the whole of the second part of the duodenum and bounded by a narrow radiolucent zone. This apparent sac-like structure varied in form from one film to another and was from time to time displaced by peristalsis to the fourth part of the duodenum. Several defects, the size of peas, were noted distally (Figs 1 and 2). Emptying of the stomach was slightly delayed.

A diagnosis of an atypical diverticulum was first considered. For confirmation contrast medium was injected through a duodenal tube into the second part of the duodenum, the tip of the tube lying in the sac (Fig. 3). No definite information was gathered from this procedure but the suggestion was made that there might possibly also be a condition of invagination.

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Fig. 1. Sac-like accumulation of contrast medium distally in the duodenum, limited by a radiolucent zone.

Fig. 2. Moderately dilated second part of the duodenum. The sac-like formation, which corresponds to an intraduodenal diverticulum has been carried into the fourth part of the duodenum by peristalsis.

On operation a soft resistance was felt on palpation of the second part of the duodenum and incision of the wall revealed a sac-like structure, ca. 8 cm long, containing a few greenish concretions. Both the outer and the inner surfaces of the sac were covered with mucosa, the ventral opening comprising about two-thirds of the intestinal circumference. Vater's papilla lay distally to the diverticular opening. The passage of intestinal contents past the sac was partly obstructed. The diverticulum was extirpated. A detailed report of the operation has been given by TURUNEN (1960).

Microscopic examination of a longitudinal portion of the sac demonstrated that it was covered with high columnar epithelium; this did not quite correspond to any particular part of the alimentary canal but most nearly resembled the duodenal wall. Proximally the mucosa was thickened, some typical duodenal glands and a few cellular elements characteristic of the bile ducts were present. Duodenal glands were very sparse in the distal four-fifths of the specimen. The diverticulum was thus a non-neoplastic structure, probably of congenital origin and best referred to the group 'intestinal duplications' (Dr. SAXÉN). The concretions in the sac consisted principally of a cellulose-like substance containing small amounts of calcium and phosphorus.

A follow-up examination six weeks after operation (Fig. 4) revealed a narrowing of the second part of the duodenum which reduced the lumen by about a third and caused slight obstruction. The patient was more or less free from symptoms.

Discussion

The duodenum may be the site of intrinsic malformations due to a diaphragm, to stenosis or to atresia (FORSSNER 1907). Most of these anomalies are revealed in infancy, only some ten cases of intrinsic duodenal diaphragm in adults

Fig. 3. Tube introduced through the stomach to fill the intraduodenal diverticulum. Barium emulsion also given by mouth.

Fig. 4. The diverticulum extirpated. The duodenum is moderately constricted at the level of opening of the diverticulum.

having been reported. TANDLER's (1900) hypothesis on the pathogenesis of such malformations is commonly accepted. He showed that in the five-week embryo the primitive gut closes solidly owing to epithelial cell proliferation. About one month later the intestinal lumen is normally restored by a process of vacuolation within the hypertrophied epithelium. An arrest of development during the time of recanalization would, according to TANDLER's hypothesis, be the cause of the malformations mentioned.

The development of an intraluminal diverticulum might be explained as a result of mechanical pressure on an already existent incomplete diaphragm. It is not inconceivable, however, that the diverticulum as such is congenital and represents a variant of duplications in the alimentary canal, such duplications generally lying collaterally. The coin which in MEYER and EDGREN's case was found in such a diverticulum had been swallowed when the patient was a child. This, as well as the findings in the present case, may perhaps support such an assumption.

The symptoms would presumably depend on the relation between the size

of the diverticular opening and the diameter of the lumen of the duodenum at this level. The extent to which the sac fills and particularly its tendency to retention are probably also of considerable clinical significance.

Intraluminal diverticula present characteristic barium meal appearances. The diverticulum appears as a contrast filled sac within the intestinal lumen and a free projection of it cannot be obtained; proximally to its opening the duodenum is dilated. The diverticular wall can often be observed in the shape of a radiolucent zone, 1 to 2 mm wide, around the homogeneous contrast accumulation of contrast medium. There is reason to look for concretions in the diverticulum.

In making the differential diagnosis the possibility of an extraluminal diverticulum should first be considered. Hypertrophic duodenal folds (MENDL & SHARP 1960) seem to produce rather bizarre appearances and should be eliminated as should polypi and invaginations, although such conditions as a rule produce the reverse roentgen appearances i. e. filling defects. In practice it is not a simple matter to arrive at a definite diagnosis.

SUMMARY

A case of intraluminal diverticulum of the duodenum is described. The mechanism of its origin and the roentgenologic differential diagnosis are discussed.

ZUSAMMENFASSUNG

Es wird ein Fall von intraluminalem Divertikel des Duodenum beschrieben und der Entstehungsmechanismus sowie die röntgenologischen differentialdiagnostischen Methoden besprochen.

RÉSUMÉ

L'auteur décrit un cas de diverticule situé dans la lumière du duodénum. Il examine le mécanisme de son origine et son diagnostic différentiel radiologique.

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CATARACT AS A LATE SEQUEL OF CONTACT ROENTGEN THERAPY OF ANGIOMAS IN CHILDREN

by

V. Bek and K. Zahn

Contact roentgen therapy of radiosensitive angiomas in children yields excellent cosmetic and functional results (1). This is important in angiomas localized in surgically difficult sites such as the eyelids and areas close to the eye. The irradiation also affects healthy tissues, some of which, especially the lens, are particularly radiosensitive; the young developing lens is more susceptible than the adult lens. It is therefore necessary to direct special attention to all possible late damage due to radiation; in the last 10 years reports on late damage following radiation therapy of benign conditions, including angiomas in children, have appeared and all emphasize the importance of employing this form of treatment with the utmost care.

The effect of ionizing radiation on the lens and the mechanism of development of radiation cataract was classically described by von Sallmann (1959) in a series of papers. The cells of the subcapsular epithelium of the preequatorial zone divide freely to form a germinal zone for the lens fibres, the proliferation of this epithelium going hand in hand with high radiation sensitivity and vulnerability. As a sequel of the destructive effect of radiation, degenerated, opaque fibres occur on the posterior pole of the lens and cataract develops. The latent period of the cataract and its degree depend on the age of the lens and dose of radiation (3). Cogan (1958) emphasized that a cataract

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may develop after doses which would cause no clinical disturbances in any other part of the body and reports 600 r to be the threshold dose for roentgen radiation (200 kV). However, many varying opinions on this problem are held (8, 9, 10, 15); according to some authors the effect of radiation on the lens may be considerably decreased by fractionation of the dose. There is, however, much experimental evidence to show that in contradistinction to the skin the effect of radiation on the lens accumulates (Poppe 1948, Ellinger 1957, Franarier & Fournier 1952).

In the abundant literature on the therapy of angiomas in children cataract is mentioned only sporadically as a late complication of treatment, mostly following radium therapy (4, 11, 17). The only more extensive study on the possibility of the development of cataract after irradiation of angiomas in children was published as late as 1959. Qvist and Zachau-Christiansen report four cases of radiation cataract in a group of 57 cases, treated with radium in early childhood 21 to 42 years previously. Most of the patients when examined had trophic changes of the skin and subcutis, the cosmetic results consequently being not entirely satisfactory. These unfavourable sequelae developed following radium therapy performed 20 to 40 years ago, at a time when the doses of radiation administered were moderately high.

In the last 20 years radium treatment has mostly been replaced by contact roentgen therapy. This is due to the technical advantages of the latter method, and above all to the ease and rapidity of its application. This method is also safer as the intensity of radiation decreases rapidly with increasing depth of the tissue, which minimizes any damage to the healthy zone below the target area.

We performed control examinations of 51 children (11 boys and 40 girls) aged between 5 and 17 years who had had contact roentgen treatment with van der Plaats' apparatus for angiomas of the eyelids (10 patients) or in close vicinity to the eyes (41 patients) with special reference to the presence of late postradiation ophthalmic changes. The classification of the angiomas in our cases was as follows: 40 cases of planotuberous and tuberonodous hemangiomas, 4 cases of haemangioma stellatum and 7 cases of teleangiectatic naevus (naevus flammeus). Treatment was performed in 40 children in their first year, in 7 during their second or third year and in four children in their sixth to ninth years. The time interval between the termination of treatment and the ophthalmologic examination was 4 to 14 years; in 47 children it was more than 6 years. This series of 51 children is a part of a larger group of 571 children with 760 angiomas treated at the roentgen clinic in the period 1945—1955. Careful consideration was paid to the cosmetic results of the treatment at the examinations; these were favourable in 90 % of our 40 cases of planotuberous and tuberonodous hemangiomas of the eyelids and areas close to the eye (18).

a b c

Fig. 1. Case 1. a) Localization and extent of hemangioma. b) Skin finding 10 years after termination of the contact roentgen therapy. c) Schema of radiation cataract.

Ophthalmologic findings: These were normal in 46 of the children. A convergent double squint was found in two of the boys but this had no relation either to a hemangioma or to its treatment. In another boy, paresis of the superior oblique muscle was present as a sequel of the surgical removal of a hemangioma in the region of the trochlea. Radiation cataract was evident in two cases.

Case reports

Case 1. E. M., girl, aged 11 years. A planotuberous haemangioma, situated in the middle of the right upper eyelid (Fig. 1a), was irradiated when the patient was 11 months old. Treatment was performed with van der Plaats' apparatus for contact roentgen therapy at 50 kV, 2 mA, FSD 2 cm, filtration 1 mm Al. Within one month a total skin dose of 1 500 r, divided into two relatively high fractions of 700 r and 800 r respectively, was applied. The right eyelid shows no pathologic or postradiation changes even at the previous site of the hemangioma (Fig. 1b). Other eye tissues were normal with the exception of the lens in which fine linear opacities in the subcapsular zone of the posterior cortex converged radially from the equator towards the lower pole. A more dense ring-shaped opacity was also present in this region through fusion of two layers of diffuse opacities, one subcapsular and another a little anterior to it, giving rise to a typical 'doughnut' appearance (Fig. 1c). The opacities were composed of many small and moderate-sized granules, fibres, and some vacuoles. The left eye was normal.

Case 2. M. M., girl, aged 7 years, who had had a planotuberous haemangioma involving the external canthus and more than half of the right upper eyelid (Fig. 2a). Treatment was begun when the child was 3 months old with van der Plaats' apparatus under the same conditions as in Case 1. Two radiation series were applied with a total skin dose of 1 800 r and 1 900 r respectively, divided into 190 to 200 r skin dose 3 times a week and an interval of 5 months between the series. The skin between the outer half of the upper eyelid and the eyebrow and the external margin of the orbit, an area of about 25 × 14 mm, was somewhat thinned (as is commonly seen following the regression of a hemangioma) and showed slight changes of pigmentation. Signs of epilation were not present and the cosmetic result was quite good (Fig. 2b). The position and function of the eyelids were normal. Other eye tissues,

a b c

Fig. 2. Case 2. a) Localization and extent of hemangioma. b) Skin finding 7 years after termination of the contact roentgen therapy. c) Schema of radiation cataract.

with the exception of the lens, show no changes. In the subcapsular zone of the posterior cortex of the lens fine opacities converged from the equator towards the posterior pole where they fused with a more irregular, dense ring-shaped opacity on the circumference of two finely opaque strata anterior to the plane of the capsule. The opacities were again composed of granules, fine fibres and some vacuoles. The subcapsular strata of the posterior cortex also showed a faint diffuse confluent opacity (Fig. 2c). The left eye was normal.

These typical radiation cataracts had very similar appearances, the differences being due only to the extent of the changes. They were found 10 and 7 years respectively after treatment in examinations aimed at the search for such sequelae. They produced no symptoms.

Discussion

The cause of radiation cataracts is presumably due to the cumulative effect of irradiation brought about by ineffective protection. The eye on the side being treated, or preferably both eyes, should be properly shielded during treatment. Protective devices may, however, be insufficient or may fail because of restlessness of the child. We formerly covered the eye with a nickel-plated lead hemispheric prosthesis, 20 mm in diameter and 2 mm in thickness. This proved to be unsuitable as it did not completely fill the conjunctival sac and tended to move, with consequent exposure of the eye to the radiation.

We have refrained from any attempt at calculating the dose of radiation absorbed by the lenses in the two cases. It would be difficult to estimate even approximately how much of the radiation was absorbed in the prosthesis and how much penetrated to the epithelium of the lens. Moreover, it will be appreciated that dosimetry in contact roentgen therapy generally is for various reasons difficult (7, 12, 13, 14).

The skin in both cases showed no changes due to radiation in spite of the fact that it received much higher doses than the lens, the latter being protected to some extent by its depth of tissue and by the prosthesis. On the other hand the lower doses of irradiation received by the lens probably accumulated to produce a radiobiologic effect. Our observations thus confirm statements that the effect of individual doses of radiation may be amassed in the lens.

The prognosis of radiation cataracts is uncertain but they usually remain stationary, their progress, if any, being very slow. Control examination of our two cases one year later showed identical findings as before.

Conclusions

Our observations indicate that radiation cataract may develop following contact roentgen therapy, which is generally believed to be safe for deeply situated tissues because of the rapid fall in the intensity of radiation with increasing depth of tissue. The high radiosensitivity of the young developing lens and adequacy of the protective devices in this technique are factors to be borne in mind if good therapeutic results are not to be marred by late sequelae. It must be stressed that in treating an angioma in a child one is dealing with a benign condition and no undue risks should be taken.

SUMMARY

Control examination of a group of 51 children, who had been subjected four to fourteen years previously to contact roentgen therapy for angiomas of or near the eyelids, revealed radiation cataracts in two of the subjects. The probable causes of the sequelae are explained and attention drawn to the precautions which are necessary in the treatment of this condition.

ZUSAMMENFASSUNG

Bei der Nachuntersuchung einer Gruppe von 51 Kindern, die vor 4 bis 14 Jahren wegen eines Angioms auf den Augenlidern oder in der Nähe derselben mit Röntgennahbestrahlung behandelt worden sind, fand man bei 2 der Kinder Katarakte. Die wahrscheinlichen Ursachen dieses Folgezustandes werden erklärt und Aufmerksamkeit wird auf die Vorsichtsmassnahmen gerichtet, die bei der Behandlung dieser Erkrankung notwendig sind.

RÉSUMÉ

Les examens de contrôle d'un groupe de 51 enfants ayant subi, de quatre à quatorze ans auparavant, un traitement par la roentgenthérapie de contact pour des angiomes des paupières ou des régions voisines ont montré une cataracte due aux radiations chez deux des sujets. Les auteurs exposent les causes probables de ces séquelles et attirent l'attention sur les précautions nécessaires dans le traitement de cette affection.

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FROM THE DEPARTMENT OF PATHOLOGY (DIRECTOR: F. WAHLGREN) AND MEDICAL CLINIC II (DIRECTOR: S. ÅKESSON), SÖDERSJUKHUSET, STOCKHOLM, SWEDEN.

MALFORMATION AND MULTIPLE STENOSES OF THE PULMONARY ARTERIES WITH PULMONARY HYPERTENSION

by

S. R. ORELL, J. KARNELL and F. WAHLGREN

In 1955, ARVIDSSON, KARNELL and MÖLLER described four cases of pulmonary hypertension of hitherto unknown cause. The patients were all young persons who had suffered from heart disease since early childhood. At angiocardiography multiple stenoses in the larger branches (2nd and 3rd order) of the pulmonary artery were demonstrated in all the cases. The authors regarded these changes as congenital anomalies.

Since the above-mentioned publication several further cases have been reported. In 1957, GYLLENSWÄRD et coll. reported 8 cases and in 1958 SMITH reported 2 cases. Similar cases have also been described by GUNNING and ELDRIDGE et coll. So far as we can ascertain no cases of this type have as yet been the subject of pathologic examination. We have, however, been able to investigate and analyse Case 2 of ARVIDSSON et coll. by means of a postmortem examination and the results are now reported.

Post-valvular stenosis of the pulmonary artery, and hypoplasia or aplasia of one entire pulmonary artery have also been described by several authors, but these cases are of another type and will not be considered.

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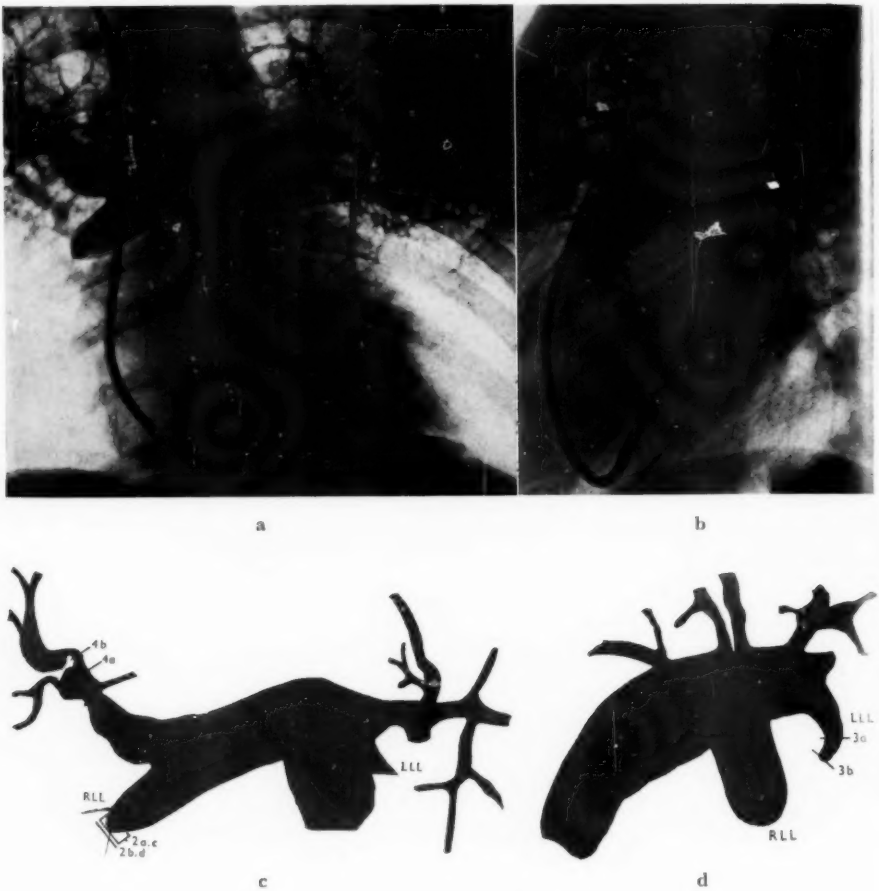


Fig. 1. Angiocardiography. a) A. p., and b) lateral, exposed simultaneously. c) and d) Schematic reproductions. RLL = right lower lobe artery. LLL = left lower lobe artery. The figures refer to the histologic sections.

Case report

U. A., female, aged 19, of normal development until the age of ten, when she became short of breath more easily than her class-mates. Her condition remained unchanged until the age of 17 when she was admitted for the first time.

Physical examination. Slender girl in apparently good health; weight 63.5 kg, height 172 cm. No dyspnoea at rest, clubbing or chest deformity. Heart: A high-pitched systolic murmur was heard at the apex. At the base of the heart there was a long, harsh systolic murmur

which also could be heard over the carotid arteries. Pulsus celer. B. P. 150/60. Blood: R. B. C. 3 mill. Hgb 84 %. W. R. neg.

Roentgen examination of the heart and lungs. The volume was 900 cc corresponding to 510 cc per sq meter body surface. The heart was moderately enlarged with preponderance of the right ventricle. There was some widening of the pulmonary trunk. The central lung vessels were wide and very irregular. The peripheral vessels were of normal size.

Catheterization. No abnormal passage could be found between the right and left sides of the heart on venous catheterization. The blood gas analyses showed no L–R shunt. The pressure measurements revealed increased pressure both in the right ventricle and the pulmonary artery. P. A. pressure 56/13 mm Hg, mean 32 mm; the pressure in the brachial artery was 143/83 mm, mean 98 mm.

Angiocardiography (Fig. 1). The pulmonary conus, the valves, and the pulmonary trunk presented a normal appearance. The right main branch of the pulmonary artery was a little wider than normal. Only the upper parts of the lungs received vessels from the pulmonary artery. No contrast filling of the lower portions, approximately corresponding to both lower lobes, the right middle lobe, and the (left) lingular lobe, was obtained. The right pulmonary artery divided into one upper and one lower branch, the latter terminating in a blind pouch approximately 3 cm from the bifurcation of the right pulmonary artery. The upper branch of the right pulmonary artery was wide and divided abruptly into several wide, irregular arteries, one of which was stenosed with a marked post-stenotic dilatation. The left lower lobe received no branches from the pulmonary artery. The artery to the upper part of the left lung was of normal width. The arborization of the pulmonary artery was of the type which is known to occur in pulmonary hypertension.

During the 2 years following this first examination no definite deterioration was discernible. After this, however, hemoptysis suddenly occurred and re-occurred six months later. The patient also began to show signs of right ventricular failure. She became increasingly short of breath and there was no improvement through confinement to bed. After progressive deterioration she was admitted to hospital again and was then in a serious condition with cyanosis, dyspnea and advanced oedema in the lower half of the body. The heart had increased greatly in size and the volume was now 1 350 cc corresponding to 710 cc per sq meter body surface. ECG which had previously only shown signs of faint right ventricular strain now showed an extremely marked right ventricular strain as in acute cor pulmonale. Incompensation was unreversible despite all treatment and the patient died from asphyxia and right ventricular failure.

Gross pathology. The heart was considerably enlarged and weighed 460 grams. The enlargement was chiefly due to hypertrophy and dilatation of the right ventricle. The wall of the right ventricle was up to 10 mm thick with an average thickness of 8 mm, while the trabeculae were considerably enlarged. The right auricle was also dilated and the walls were somewhat thickened. The left ventricle was of about normal size with a wall thickness of some 12 mm. The left auricle was normal. The ventricular septum was normal and the foramen ovale was closed. The ostia and valves of the heart, including the pulmonary ostium, were unchanged. The large vessels left the heart in a normal manner. The ductus arteriosus was closed. The aorta and its main branches were of normal width and were generally of a normal appearance.

The pulmonary trunk and both of the main branches were possibly slightly dilated but followed the normal course. The intima showed an irregular thickening in the form of yellowish, fairly large and often confluent plaques which gave a mottled appearance to the inner walls of the vessel. More peripherally the walls of the main branches and the lobar arteries were wrinkled, principally longitudinally.

In the left pulmonary artery just before the bifurcation there was a transverse crease formation on the posterior wall. This crease formation was low and occupied only about half

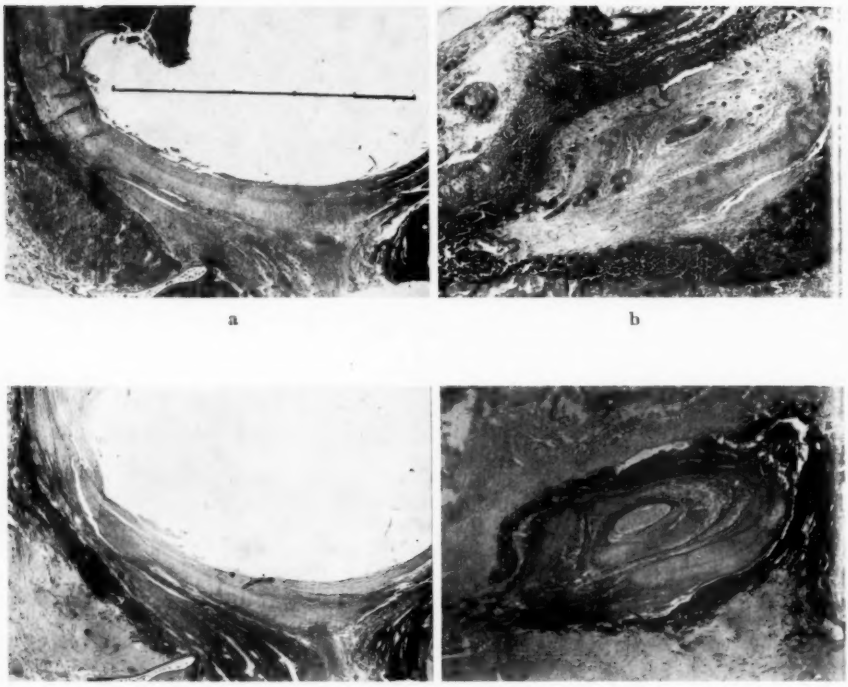
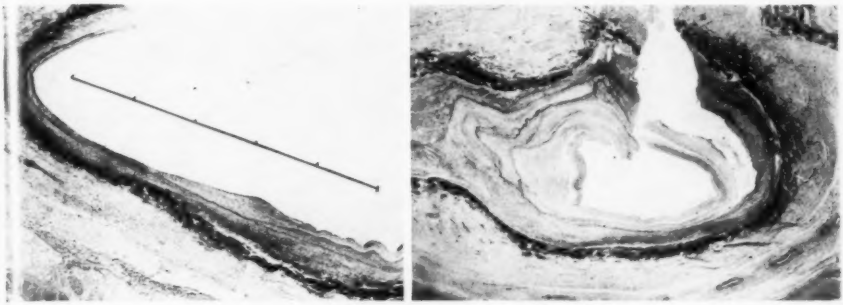


Fig. 2. Right lower lobe artery. Longitudinal sections (a and c) through the blind pouch, and transverse sections (b and d) immediately distal to the former. a) and b) Van Gieson; c) and d) Weigert's elastic stain. × 17. The scale equals 5 mm.

of the vessel's circumference. It did not result in any serious constriction of the lumen. Peripherally around this, however, the lower lobe artery narrowed off swiftly in a funnel form so that its lumen was reduced over a distance of a few centimetres by more than half. More peripherally in the left lower lobe the pulmonary artery branches were extremely thin, entirely obliterated and had the appearance of solid tissue strands. The proximal part of the left upper lobe artery lumen was narrower than normal, this apparently being due to the fact that the wall of the vessel was markedly wrinkled longitudinally. More peripherally the majority of its branches were wide and thin-walled, though some of the branches in the basal segment were, like the lower lobe branches, very thin and totally obliterated.

The right pulmonary artery bifurcated normally. The proximal part of the lower lobe artery was some 15 to 20 mm thick. It was filled up as far as the bifurcation with a clot which was partly fresh and partly organized. The lower lobe artery lumen terminated in a blind pouch 30 to 35 mm from the right pulmonary artery bifurcation. In its continued course the outer circumference of the artery was approximately 5 × 10 mm and the lumen was completely obliterated. Proximally the right upper lobe artery lumen was fairly wide,



a b

Fig. 3. Sections through narrowing portion of left lower lobe artery. The distance between (a), proximally, and (b), distally, is less than 10 mm. Weigert's elastic stain. × 17.

but further out it narrowed since the wall was wrinkled. In one of the thicker branches, 35 to 40 mm from the bifurcation, there was a limited diaphragmatic stenosis and peripherally around this there was a certain post-stenotic dilatation. The majority of the other branches of the right upper lobe were considerably thinner than usual and in places completely obliterated.

The entire right middle lobe artery was very thin with a narrow lumen, but there was no complete stenosis and the lumen could be traced far out into the lung.

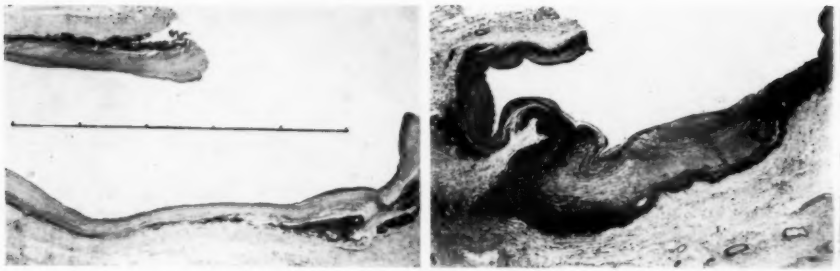
The lung veins followed the normal course and discharged into the left auricle. The walls, however, were somewhat thickened and the lumen narrower than usual, particularly in the lower lobe veins.

On both sides there were loose accretions between the pleural sheaths, mainly at the level of the lower lobes. The lungs were of average size and somewhat heavier and firmer than usual. In the upper lobes the lung tissue was light greyish-red and normally aeriferous, in the lower lobes it was considerably darker and only slightly aeriferous. There was no infarction and no signs of pneumonia. The trachea and the bronchial tree were normal.

The parenchymatous organs showed signs of chronic stasis. There were a few hundred ml of transudate in the abdominal cavity and considerable subcutaneous oedema of the legs. The systemic circulation arteries showed no arteriosclerotic changes. Apart from the changes which have been described in the pulmonary arteries, there were no other vessel anomalies and no malformations in general.

Microscopic examination. The heart and lungs were removed together during the postmortem and put into 5 % formalin. After fixation small segments were removed from various parts of the pulmonary arterial tree and from the lung parenchyma for paraffin embedding and sectioning. The sections were stained with van Gieson's stain, hematoxylin-eosin and Weigert's elastic tissue stain. Some of the sections were also stained by the Ladewig method. A number of arterial segments were examined by serial sectioning.

In the pulmonary trunk and both of the main branches varying degrees of intimal thickening, sometimes exceeding the thickness of the media were found. The thickened intima consisted of loose acellular connective tissue, fairly rich in collagen and containing a small quantity of fine elastic fibrils. Here and there were large, atheromatous plaques with extensive deposits of cholesterine in the deeper parts of the intima. The media was of normal thickness and



a b

Fig. 4. Stenosed main branch of right upper lobe artery. a) Proximally to stenosis, b) through diaphragmatic stenosis. Weigert's elastic stain. × 17.

regular structure with only slightly fragmented elastic laminae. Further out in the main branches there was an evident increase of collagen in the deeper parts of the media (Fig. 5c).

In the lobar pulmonary arteries considerable fibrous intimal thickening was visible. In general, this showed a manifest stratification marked by quite distinct, elastic laminae. The media was of varying thickness and was for the greater part considerably thinner than usual. The elastic laminae of the media were extremely irregular and fragmented or clumped together. The outer parts of the media consisted of compact, coarse, acellular collagen connective tissue (Fig. 5b).

The macroscopically obliterated pulmonary artery branches of 2nd and 3rd order were much thinner than normal. In most cases they had an irregular formation in cross-section. The media was thin and revealed the same pathologic structure as described above. The outer part of the wall consisted of compact collagen connective tissue. The lumen was completely or almost completely obliterated by a loose, fairly acellular connective tissue. This connective tissue was divided up into several layers by concentric elastic laminae, similar to the year rings in a tree (Figs 2d, 3b). Between the laminae there was a small quantity of fine elastic fibrils and in places in the obliterating connective tissue one or more fine lumina containing red blood corpuscles were noted. This corresponded to what can be seen in the recanalization of organized thrombosis (Fig. 2b). In some places the connective tissue also contained a few inflammatory cells. Fresh thrombosis was visible only in the proximal wide section of the right lower lobe artery. Similar changes were observable even out in the smallest pulmonary artery branches of the elastic type, although obliteration was less marked here than in the larger proximal arteries.

The following arterial segments were examined in serial sections.

In the left pulmonary artery the earlier mentioned crease formation near the bifurcation marked the point of change from a normal to a pathologic wall structure. The actual crease was created through the limited thickening of the media, the elastic tissue of which was fragmented and irregular. There was also a considerable increase of collagen in the media in this area. The funnel-like narrowing of the lower lobe artery was observable through the transverse serial sectioning. Most of the obliteration was brought about by layers of connective tissue on the intima, but the external circumference of the vessel also decreased by about 50 % in the 1 cm long segment which was examined. The vessel wall showed the pathologic structure described above (Fig. 3).

The right lower lobe artery was examined in longitudinal sections through the blind pouch with an immediately adjoining transverse section. Proximal to the stenosis the lumen was

a b c

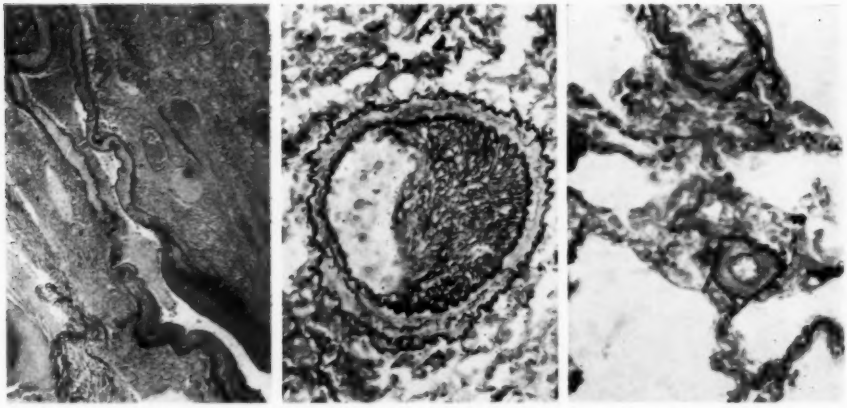
Fig. 5. a) Pulmonary artery of 2nd order in a case of recurring emboli. Stratified intimal thickening and normal media. b) Left lower lobe artery of the actual case. Stratified intimal thickening and pathologic media. c) Right pulmonary artery of same case. Atheromatous intimal thickening and principally normal media. Weigert's elastic stain. × 41.

of normal width. The clot in the lumen was partly fresh, partly organized. The intima was thickened and the media was of the same pathologic structure as described earlier. The change from normal to abnormal structure in the vessel wall occurred near the bifurcation of the right pulmonary artery, though it was not so clearly marked as on the left side. At the stenosis the outer diameter of the artery diminished rather abruptly and here, too, the compact connective tissue in the outer part of the vessel wall was most abundant. The stenosis, which was total, was brought about by layers of connective tissue on the intima. Distal to the stenosis a very narrow lumen had been re-formed by recanalization (Fig. 2).

Serial sectioning through the stenosis in one of the thicker branches of the right upper lobe artery showed that the stenosis resulted from a deep, longitudinal wrinkle which was bridged by a layer of loose connective tissue on the intima. The stenosis was situated near the branching-off point of a lesser branch. The vessel wall showed a similar structure as the other arterial segments described (Fig. 4).

The peripheral pulmonary arteries of the muscular type quite often revealed varying degrees of obliteration, brought about by fibrous intimal thickening. This thickening was in some regions concentric while in others it was limited to one sector of the cross-section (Fig. 6b). The entirely obliterated vessels in places showed signs of recanalization, occasionally with several small lumina. The intimal thickening in the small arteries was present to the same extent in the upper lobes as in the lower lobes. Within the upper lobes the arterioles and the small muscular arteries often showed, too, a fairly marked hypertrophy of the media and perivascular fibrosis (Fig. 6c). In the lower lobes the arterioles were not definitely changed though the muscular arteries showed certain hypertrophy of the media.

The bronchial arteries were manifestly larger than normal and seemed to be larger in the lower lobes than in the upper lobes. In general they had a normal microscopic structure, though in places they revealed a slight fibrous intimal thickening. In a section from the right lower lobe it was possible to observe a wide anastomosis between a fairly large bronchial



a b c

Fig. 6. a) Anastomosis between bronchial artery and pulmonary artery of elastic type. The pulmonary artery (bottom right) shows stratified intimal thickening and pathologic media. Weigert's elastic stain. × 41. b) Peripheral pulmonary artery of muscular type with an external diameter of about 170 μ obliterated by fibrous intimal thickening. Weigert's stain. × 435. c) Arteriole in a section from upper lobe. External diameter about 42 μ, internal about 18 μ. The vessel has a markedly hypertrophic muscular media. Weigert's stain. × 435.

artery and a pulmonary artery of the elastic type with fibrous intimal thickening and a pathologic media. The bronchial artery was histologically essentially normal with distinct internal and external elastic laminae and only slight intimal thickening. The anastomosis was situated in the outer fibrous part of the wall of a large bronchus. Serial sectioning gave the impression of a fairly wide side-to-side anastomosis surrounded by coarse fibrous tissue. No actual inflammatory changes were seen (Fig. 6a).

The pulmonary veins were thinner than usual, particularly those in the lower lobes. The vein walls were somewhat thickened and the outer parts were sclerotic, but otherwise they were normal.

The parenchyma of the lower lobes was the seat of extensive atelectasis, oedema and bleeding. Within the upper lobes there was marked emphysema alternating with atelectasis. The alveolar septa were generally thickened with collagen increase, and the pleurae were also thickened. Subpleurally in the lower lobes there were numerous bunches of muscular vessels which often showed more or less marked medial hypertrophy. Subpleural vessels were considerably sparser in the upper lobes.

Discussion of the pathologic findings. As was mentioned at the beginning multiple stenoses of the peripheral pulmonary arteries have been diagnosed in children and young persons who have had symptoms of heart disease since early childhood. This of course indicates that the changes are principally of a congenital nature. At the same time it seems extremely likely that added to the congenital vessel anomalies are changes secondary to the increasing pressure in the lesser circulation and changes secondary to thrombotic complications. It is thus questionable to what extent the pulmonary artery changes are primarily congenital.

The results of the pathological investigation of our case can be summed up in the following points:

1. The vessel wall in the pulmonary trunk and the two main branches showed marked atheromatous thickening of the intima, but were otherwise of a principally normal structure.

2. The vessel walls in the lobar pulmonary arteries and their branches of the elastic type were of an unmistakably pathologic structure beyond the point of bifurcation of the main pulmonary arteries, particularly as regards the elastic tissue of the media.

3. In the lobar lung arteries and their branches of the elastic type the lumina were to a great extent obliterated by fibrous intimal thickening which was divided by concentric elastic laminae into several layers. The entirely stenosed arteries were often recanalized.

4. The outer diameters of the obliterated peripheral pulmonary arteries were also considerably smaller than usual.

5. The bronchial arteries were larger than normal, especially in the lower lobes. In the right lower lobe there was an anastomosis between a bronchial artery and a pulmonary artery of the elastic type. Subpleurally a large number of muscular vessels was observed, particularly in the lower lobes.

6. Pulmonary arteries of the muscular type and arterioles were often obliterated through fibrous intimal thickening. In the upper lobes in particular vessels of this calibre also revealed quite considerable hypertrophy of the media.

In our opinion the most important aspect of the case under review is the peculiar pathologic structure in the media in the lobar pulmonary arteries and their branches of the elastic type. So far as we know no similar changes occur in other forms of pulmonary hypertension, nor in connection with older, organized thrombo-emboli in the pulmonary arteries. We have interpreted these changes in the media as a malformation, principally of the intrinsic elastic tissue. The extremely diminished calibre of the lower lobe arteries and some of the upper lobe branches can scarcely be merely secondary to the marked increase of collagen tissue around the vessels, but must be regarded as a congenital hypoplasia.

The stenoses and the obliterations in the lower lobe arteries, and also in some of the upper lobe branches, were brought about by fibrous intimal thickening which was often divided up into several layers by concentric elastic laminae like the year rings in a tree. Similar pictures are observable in cases of recurring pulmonary emboli which have organized and merged with the vessel wall (Fig. 5). Since several arteries which were stenosed in this way also revealed appearances which were in complete agreement with those seen in recanalization of organized thromboses, we have come to the conclusion that intimal thickening and the resultant stenosis is the result of secondary, recurring thromboses in the anomalous pulmonary arteries.

The obliteration of both of the lower lobe arteries appears to have brought about increased collateral circulation via the bronchial arteries. These were

larger than normal and seemed to be more strongly developed in the lowe lobes than in the upper lobes. The side-to-side anastomosis between a bronchia artery and a fairly large pulmonary artery of the elastic type which was foun close to a large bronchus in the right lower lobe, is also an indication of in creased collateral circulation. It seems possible that a reversal of flow in th peripheral pulmonary arteries might have taken place through anastomose of this type (LIEBOW 1950, 1960). The lack of thrombotic changes in th bronchial artery, and the fact that the smaller elastic arteries were less oblite ated than the main lobar arteries, seem to be in agreement with this hypothesi The numerous muscular vessels situated subpleurally in the lower lobes ca also probably be regarded as collaterals.

The changes in the peripheral pulmonary arteries of the muscular typ and in the arterioles are also of considerable interest. The small muscula arteries showed more or less marked hypertrophy of the media and ofte fibrous intimal thickening with obliteration of the lumina as well. Obliterate vessels often presented signs of recanalization. The intimal thickening is probably of a thrombotic nature like the corresponding changes in the pulmonary arteries of the elastic type. Concerning the arterioles, so far as could b ascertained without quantitative examination, there was a difference betwee the upper lobes and the lower lobes. In the upper lobes the arterioles ofte revealed considerable medial hypertrophy and perivascular fibrosis, while th lower lobes showed no such manifest changes. This can be interpreted as a expression of a difference in pressure conditions between the upper and th lower lobes.

General discussion

The case which has been described was one of a young woman who suffered from pulmonary hypertension. The postmortem revealed changes in the loba pulmonary arteries with branches of a nature which has not previously been described. This implies a hitherto unknown cause for pulmonary hypertension. These pulmonary artery changes in our opinion were brought about partly by the malformation of the vessel walls, particularly the elastic tissue of th media, and partly by secondary thrombotic disease. The vessel wall malformation had its beginning approximately at the bifurcations of the left and right main pulmonary arteries.

The case thus shows a strong similarity with another of the cases published by ARVIDSSON et coll. (Case 1) in which there were multiple partial stenoses in the lobar pulmonary arteries near the bifurcations of the two main arteries. Thus both cases indicate that the two main branches of the pulmonary artery, and the lobar arteries with their branches, have a different embryonic origin or at least belong to different phases in the embryonic development. It is known that the two main branches develop from the sixth aortic arch, while the details of the embryonic development of the peripheral pulmonary arteries are, so far as we can ascertain, not known.

But in one essential aspect the cases are different. In one case the pulmonary arteries peripheral to the stenoses, at least judging from the roentgenologic examination, appeared to be normal. In the case described in this paper, however, the pulmonary arteries in the lower lobes and also to a certain extent those in the upper lobes were obliterated peripheral to the stenoses, not only because they were secondarily thrombosized but also because they were hypoplastic as judged from the diameter of the media. This difference between the two cases is of great significance from the clinical viewpoint. In cases with partial stenoses, such as Case 1 of ARVIDSSON et coll., it is probably possible to remove the obstruction to the blood-flow and lower the pulmonary artery pressure by an operation, while surgical correction is impossible in cases of the type described here. If in such cases it proves impossible to show through angiocardiography that there is a lumen peripheral to the stenoses, then it can be fairly well assumed that there is in fact no lumen and that the case is consequently not suitable for surgical treatment.

SUMMARY

The authors describe and discuss the postmortem findings in a case of malformation of the pulmonary artery and its branches with pulmonary hypertension. This was Case 2 of the series of four cases of this condition previously described in this journal.

ZUSAMMENFASSUNG

Die Autoren berichten und besprechen die postmortalen Befunde eines Falles von pulmoneller Hypertension als Folge einer Missbildung der Arteria pulmonalis und ihrer Äste. Dies war der Fall 2 einer Serie von vier Fällen dieses Krankheitsbildes worüber früher in dieser Zeitschrift berichtet wurde.

RÉSUMÉ

Les auteurs décrivent et étudient les constatations nécropsiques dans un cas de malformation de l'artère pulmonaire et de ses branches avec hypertension pulmonaire. Il s'agit du cas N° 2 de la série de quatre cas de cette affection décrits antérieurement dans ce journal.

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CANCER OF THE MIDDLE EAR AND MASTOID

by

HENNING SØRENSEN

The purpose of the present study was to show that it is possible to obtain permanent cure in cancer of the middle ear and mastoid in a considerable number of cases by radiotherapy combined with radical removal of the tumour tissue under microscopic control. The investigation was concerned only with cancer of the middle ear and mastoid and did not comprise malignant neoplasms of the pinna or the external auditory meatus.

Diagnosis. In all studies on cancer of the middle ear it is emphasised that early diagnosis is of great importance (FIGI and WEISMAN 1954, BRADLEY and MAXWELL 1954 and LINDAHL 1955), since surgical cure is much easier to attain as long as the tumour is relatively small, while the intervention is much more complicated in cases with extensive involvement.

The clinical picture and symptomatology are described in detail in studies comprising large series (FIGI and HAMPSTEAD 1943). It is emphasised that all symptoms of cancer of the middle ear are the same as may be encountered in chronic otitis media, and that the difficulties in making an early diagnosis are further increased by the fact that most cases of cancer of the middle ear and mastoid occur in patients with chronic otitis media. These observations are made in most papers on cancer of the middle ear, which suggests that the chronic suppuration may be of aetiologic significance. However, some authors (FIGI and HAMPSTEAD; BRADLEY and MAXWELL) found chronic otitis media only in a minority of their patients, and BRADLEY and MAXWELL expressed

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the view that the discharge is a doubtful factor in the aetiology. In short, cancer of the middle ear and mastoid does not present any characteristic early clinical manifestations, and the examiner must therefore to a great extent rely on his judgment and experience as to the course of chronic otitis media. It is a change in the course of the condition which may be an indication that malignancy has developed. The final diagnosis should obviously be made by the histologic examination of a biopsy specimen.

Malignancy most frequently manifests itself by the recurrence of polypoidal or granulation-like tissue, often of a tough and firm consistency, and easy bleeding. Cancer of the middle ear associated with cholesteatoma is reported to be rare (BRADLEY and MAXWELL). Recurrent polyps should therefore always be examined histologically in order to exclude the presence of cancer.

Bleeding from the ear is presumably the most significant symptom; it may occur early in cancer, and is relatively rare in chronic otitis media.

Pain is also a characteristic symptom. The pain, which is localised to the ear and often radiates to the neck, may become very intense and then presents great therapeutic difficulties; intense pain is suggestive of extensive involvement.

Facial palsy occurs if the tumour invades the bone. This sign is also relatively frequent, but not one of early occurrence.

A distinct aggravation of hearing impairment or the occurrence of vestibular signs in patients with chronic otitis media may be one of the first indications of the development of cancer.

Roentgen examination of the temporal bone may reveal osseous destruction although this shows no particular characteristics; however, the extensive osseous destruction sometimes present in cancer is rarely seen in otitis media.

Histology. Carcinoma is by far the most frequent malignant tumour of the middle ear. Prickle-cell carcinoma is most common, but the basal-ceil variety may also be encountered; adenocarcinoma is very rare. Sarcomata are uncommon and usually occur in younger subjects.

In 1945, ROSENWASSER described the first case of a glomus jugulare tumour of the middle ear. Since then, more than 100 cases of this type of cancer, which arises from the jugular fossa, have been reported. Histologically, this tumour consists of greatly vascularised tissue, in which clusters of uniform epithelioid cells are seen. Few mitoses are present and the tumour is usually not considered to be histologically malignant; it may, however, give rise to destruction of the temporal bone, and metastases have been observed in a few cases. Re-appraisal of tumours which has previously been classified as angiosarcomata or haemangioendotheliomata has shown that they actually were glomus jugulare tumours.

Treatment. The most common method of treatment has for many years been, and still is, a combination of radiotherapy and resection of the mastoid and middle ear. However, the tumour has often invaded the temporal bone,

in which case this type of surgical intervention is not sufficient. The operative cavity must be extended and the infiltrations must be followed through the bone in an attempt to remove the tumour tissue radically.

During recent years, en bloc resection of the temporal bone with simultaneous dissection of the cervical lymph nodes has been given a trial (WARD, LOCK and LAWRENCE 1951, CAMPBELL, VOLK and BURKLUND 1951, PARSONS and LEWIS 1954, 1958). By these operations, some patients with extensive malignant tumours involving the temporal bone have been cured.

In contrast to this very radical surgery, BOLAND and PATERSON (1955) emphasised the advantages of radiotherapy; they obtained a cure in 6 of 27 patients by means of radium irradiation alone. Multiple fields and a beam direction giving a high dose level in the petrous part of the temporal bone were used. The complications of this therapy are irradiation damage to the brain stem and bone necrosis.

Prognosis. Cancer of the middle ear and mastoid is a rare condition. Few large series are available which could form the basis for the evaluation of the prognosis.

Among 73 patients with cancer of the middle ear, FIGI and WEISMAN (1954) had only 13 who were free from recurrence after the lapse of 2 to 3 years. BRADLEY and MAXWELL (1954) obtained only two five-year survivals among 35 patients.

LINDAHL (1955) had collected 89 cases of cancer of the middle ear from the literature from 1939 onwards, mainly from British and American journals. Of these, only seven survived for more than 5 years. His own series consisted of 16 patients of whom four were cured. Among the measures which LINDAHL suggested in order to improve the outlook for patients with this malignant and often very painful condition was centralisation of the treatment to a few departments which have all available radiotherapeutic aids and an otologist with a special interest in surgery of the temporal bone; such an otologist would then gain wide experience in the treatment of the condition. The danger involved in this centralisation is that others get out of touch with or actually 'forget' the condition; hence the chances of early diagnosis, which is of great therapeutic importance, may be reduced.

Personal investigations

During the period 1939—1953, 12 patients were admitted to the Radium Centre and the University Ear Clinic with a diagnosis of cancer of the middle ear and/or mastoid. They consisted of 6 men and 6 women, whose ages ranged from 44 to 75 years. In 10 of the patients the cancer developed during the course of chronic otitis media; only 2 of the patients had not previously suffered from aural discharge.

Table 1

Case	Sex	Age (years)	History	Site of origin	Histological diagnosis	Result
1	F	67	Chronic otitis media with discharge from both ears since childhood. Pain in left ear and dizziness for 7 months.	Intrinsic	Prickle-cell carcinoma	Died after 3 months
2	F	41	Eczema of right ear with discharge since childhood. Radiating pain and increasing discharge from the right ear for 6 months.	Extrinsic	Prickle-cell carcinoma	Died after 15 months
3	M	54	Discharge from left ear, with pain, hearing impairment and dizziness, for 2 years.	Intrinsic	Prickle-cell carcinoma	Died after 14 months
4	M	75	Small nodule in the left external auditory meatus for 15 years. Growth of tumour, with discharge and bleeding, for 4 years.	Extrinsic	Basal-cell carcinoma	Died after 2.5 years; no signs of recurrence
5	M	56	Recurrent otitis media since childhood. Radical operation on right ear at age of 19. Bleeding from the cavity for 9 months.	?	Prickle-cell carcinoma	Survived for more than 5 years
6	F	54	Pain in the right ear for 3 years.	Extrinsic	Basal-cell carcinoma	Survived for more than 5 years
7	M	63	Discharge from both ears since childhood. Increasing discharge and intense pain for 12 months.	Intrinsic	Prickle-cell carcinoma	Survived for more than 5 years
8	F	47	Abscess behind the right ear and pain for 1 month.	Intrinsic	Prickle-cell carcinoma	Survived for more than 5 years
9	F	53	Periodic discharge from the left ear for 44 years. Facial palsy, pain and haemorrhagic discharge for 2 months.	Intrinsic	Prickle-cell carcinoma	Died after 22 months
10	F	59	Periodic discharge from the left ear for 8 years. Increasing discharge, pain and hearing impairment for 1 month.	Intrinsic	Prickle-cell carcinoma	Survived for more than 5 years
11	M	57	Periodic discharge from right ear since childhood. Increasing discharge for 12 months.	?	Prickle-cell carcinoma	Died after 6 months
12	M	48	Periodic discharge from both ears for 25 years. Intense pain in left ear for 3 months.	Intrinsic	Sarcoma	Died after 3 months

The histories are briefly given in Table 1, in which it is also shown whether the tumour was extrinsic or intrinsic, i. e. whether the tumour had arisen in the external auditory meatus and had later invaded the surrounding structures, or whether it had primarily arisen in the middle ear or mastoid. This classification is mainly of academic interest. It is sometimes impossible to determine the site of origin of the lesion, especially if it has become very widespread. In most cases, the classification was based on an assessment of the past history

and the operative findings. All cases in which the lesion was confined to the external auditory meatus were excluded.

A survey of the symptoms and signs are given below. In 7 cases, the aural discharge had been blood-stained. Most of the patients suffered from impaired hearing due to otitis media, but in several cases further impairment occurred at the time when a change in the condition suggested cancer. It is characteristic of the pain that it was often intense and radiated especially to the neck as well as to the temporal and occipital regions. Facial palsy was present in one patient pre-operatively, but in 7 additional cases it occurred after the operation, usually because the facial nerve had become either completely or partially surrounded by tumour tissue and therefore could not be preserved.

Symptoms and signs	No. of cases
Aural discharge	10 (7 bloodstained)
Impaired hearing	11
Pain	11
Facial palsy	1 (+ 7)
Dizziness	4
Dysphagia	3
Granulations	11
Palpable cervical nodes	2

The presence of enlarged regional lymph nodes need not necessarily imply that they are sites of metastases. Metastases from cancer of the middle ear occur at a late stage.

Roentgen examination of the temporal bones showed no definite signs of destruction in 6 cases, whereas more or less definite necrosis of the middle ear, mastoid or external auditory meatus was seen in the remaining 6 cases. The roentgenograms revealed extensive destruction of the entire petrous bone in 3 cases; in one of these the zygomatic process was also involved.

Treatment

All the patients were treated with a combination of radiotherapy and surgery. A review of the case records showed that the treatment had varied to some extent, for which reason it is difficult to survey it in tabular form. These variations were principally due to the fact that some of the patients had already received some treatment before admission. Operation had previously been performed in 6 patients, while the remaining 6 were admitted without preceding treatment, and subjected to operation. The former 6 were given postoperative radiation therapy, while some of the latter had pre-operative roentgen therapy and all of them received postoperative radium irradiation.

Data relating to the radiotherapy are shown in Table 2. The roentgen irradiation was delivered at a voltage varying from 160 to 180 kV. In all cases except one, a Thoraeus filter (HVL 1.5 Cu) was used. The depth doses were calculated from free air doses by means of the tables of Wachsmann and Dimotsis. In these calculations the depth of the tumour was invariably taken as 4 cm.

In the postoperative radium therapy, radium, usually placed in Heymann tubes, was inserted into the cavity immediately after the removal of the tumour. The tubes, packed in gauze, were placed irregularly in the cavity. However, other forms of tubes and packing were also used, for which reason the treatment in the analysis seemed relatively heterogeneous

Table 2

Case	Roentgen				Radium		Total (r)
	Field (sq. cm)	Focus-skin distance (cm)	Duration of treatment (days)	Depth dose (r)	Mg/hours	Dose (r)	
1	50	70	40	4 857			4 857
2	50	50	29	4 450			4 450
3	—	—	—	—	1 050	8 400	8 400
4	—	—	—	—	720	4 000	4 000
5	—	—	—	—	135	832	832
6	—	—	—	—	180	832	832
7	100	50	30	4 290		—	4 290
8	100	50	25	3 744	300	2 960	6 704
9	75	50	27	3 795	160	1 840	5 635
10	100	50	9	1 435	1 090	3 700	5 135
11	75	50	28	4 125			4 125
12	80	40	10	800	280	648	1 448

and was therefore difficult to evaluate. The irregular shape of the cavity in itself made it impossible to state the exact tumour dose.

The number of milligramme-hours given in the individual cases are recorded in Table 2. In order to estimate the dose as expressed in roentgens the following experiment was performed (for results, see Table 3): A varying number of Heymann tubes, packed in gauze in the same way as when inserted into the operation cavity, were immersed in water in a 3-litre beaker. The irradiation was measured by means of a Siemens gammameter, (1) close to the sides and tips of the tubes, and (2) at a distance of 0.5 cm from the tubes. A similar principle has previously been used by BENNER (1941). The results given in Table 3 are the average values of five measurements. It is seen that the irradiation increases with the number of tubes up to three, but then no further increase occurs. In Table 2, the results obtained in measurements on the surface of the tubes (average of side and tip) are used.

The experiment obviously gives only a rough estimate of the dose, since, as already pointed out, the irregular distribution of the irradiation makes it impossible to determine the exact dosage, but it certainly indicates that in the calculation of the dosage attention must be paid to the fact that the use of a large number of tubes does not materially increase the irradiation, since the tubes will then 'eclipse' one another.

A comparison of the total doses and the long-term results did not reveal any correlation. However, the series is too small for definite conclusions as to the effects of details in the treatment.

The operation is performed under general anaesthesia. When the mastoid process has been resected and access to the middle ear is free after removal of the bridge, the cavity is inspected under the microscope. Tissue suspected of malignancy is submitted to histologic examination (frozen sections), and radical dissection of all tumour tissue is made under microscopic control. Even in the presence of a very extensive lesion, it is possible to follow the tumour throughout the petrous bone, including the apex. In one case, the entire bony labyrinth had loosened and lay as a sequestrum surrounded by tumour tissue (the capsule of the labyrinth seems to be greatly resistant to tumour). Even

Table 3

Dosage rate for various arrangements of tubes

No. of HEYMANN tubes 10 mg each	Sites of measurements			
	On surface of tube		0.5 cm from tube	
	Side (r/h)	Tip (r/h)	Side (r/h)	Tip (r/h)
One.....	110	25	56	17
Two.....	185	56	80	42
Three	225	100	100	65
Four.....	225	125	100	60

in the presence of invasion of the eustachian tube, around the jugular vein, or of the parotid gland, zygomatic process or mandibular joint, the tumour has been successfully removed, and radical removal checked by repeated examination of frozen sections.

A doubtful area of the dura may be resected, and the defect closed by a fascial graft.

The description of the operation in a 56-year-old patient with a prickle-cell carcinoma, which had arisen in the cavity from a previous radical operation, may serve as an illustrative example.

A large retro-auricular incision was made, and the pinna turned down. After chiselling off the confines of the old operation cavity, the entire contents of the middle ear and the old cavity were removed. The intact facial ridge then became visible; towards the promontory there was osteitis of the wall above the facial nerve. The oval window was normal, but the stapes was missing; the footplate of the stapes was freely movable. The round window and the promontory were normal. Around the tensor tympani and towards the dura there were probable areas of osteitis; the bone was therefore removed, by which the dura of the middle cranial fossa was uncovered to a great extent. Tumour tissue was present, particularly in the anterior part of the middle ear (frozen sections). The bone was then removed to the mandibular joint, giving free access to the cavity extending in front of the promontory towards the apex and around the eustachian tube. All tumour tissue was removed by means of a curette. It was now seen that the internal carotid artery was exposed for a considerable distance, and that the cavity extended in front of and behind this artery. After the removal of all doubtful tissue, radium tubes were placed in the cavity (ANDERSEN).

Results and Discussion

No immediate postoperative deaths occurred. Six of the 12 patients died from the neoplasm from 2 to 22 months after operation, all revealing signs of intracranial tumour invasion; neurologic manifestations, such as paralysis of the soft palate or the hypoglossal nerve, meningitis or ataxia, developed. One patient died $2\,^1/_2$ years after operation from cardiac disease, but without signs of recurrence of the tumour. The remaining 5 patients survived for more than 5 years without recurrence.

It is worthy of note that recurrence of the neoplasm was not seen in any of the patients after the lapse of the first 18 to 24 months. The periods of observation for the 5 patients in whom the tumour did not recur are 8, 6 1/2, 6, 5 and 5 years.

The frequent occurrence of chronic otitis media in our cases suggests that long-standing suppuration is of aetiologic significance and underlines the importance of careful observation of patients with this condition, especially if granulation tissue or polyps are present. If the course of the otitis changes, repeated biopsies should be performed. In conformity with other reports on malignant tumours of the temporal bone, the histologic diagnosis was in most cases of the present series one of prickle-cell carcinoma.

The results of treatment show that radical excision combined with radiotherapy is valuable even when the lesion is widespread. In cases in which a complete cure could not be obtained, it was nevertheless possible to alleviate the pain by surgical measures which were not grossly mutilating.

As is evident from Tables 1 and 2 no correlation between the total doses and the long term results could be demonstrated. In 3 patients (Cases 5, 6, and 12) the doses were definitely inadequate; 2 of these survived for more than 5 years and thus were cured by the operation alone while the third patient (Case 12), in whom the operation had not been radical, died. Large doses were given in 5 cases (Cases 3, 4, 8, 9, and 10); two of these patients survived while 3 died, presumably because the tumor had invaded tissue far from the operation field. In the remaining 4 patients (Cases 1, 2, 7, and 11) it is doubtful whether the doses applied had been adequate; only one of these survived. Although the series is too small for definite conclusions as to the effect of the radiotherapy, it seems likely that larger doses in Case 12 and the last group might have improved the results obtained.

Some of the important anatomic structures in this region may be spared by the method described. This cannot be done by the en bloc dissection (i. e. resection of the entire temporal bone with or without dissection of the cervical lymph nodes) performed by WARD et coll., CAMPBELL et coll., and PARSONS and LEWIS. With regard to the metastases to the cervical lymph nodes, constituting one of the reasons why en bloc dissection is performed, it must be considered (1) that enlarged cervical nodes do not necessarily imply that they are invaded by metastases, and (2), as emphasised by BRADLEY and MAXWELL, that in patients with palpable metastatic cervical nodes deep extension by way of the peritubal lymphatics is likely, for which reason removal of the involved cervical nodes would be ineffective.

Radiotherapy alone, as suggested by BOLAND and PATERSON, does not seem to be superior to radical operation combined with radiotherapy. Furthermore, the high dose level which is required by this method may give rise to irradiation damage of the brain stem, or to bone necrosis, which will necessitate subsequent surgical treatment.

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SUMMARY

The treatment of malignant tumours of the middle ear and mastoid by radical operation, n combination with roentgen and radium irradiation in a series of 12 cases, is described and discussed. Five patients were free from recurrence for more than 5 years, one died without signs of recurrence 2 $^1/_2$ years after operation, and six died from recurrence of the tumour.

ZUSAMMENFASSUNG

An Hand einer Serie von 12 Fällen wird die Behandlung von malignen Tumoren des Mittelohrs und Mastoids mittels Radikaloperation, kombiniert mit Röntgen- und Radiumbestrahlung, beschrieben und näher besprochen. Fünf Patienten waren mehr als 5 Jahre ohne Rezidiv, einer starb ohne Anzeichen eines Rezidives 2 $^1/_2$ Jahre nach der Operation und 6 starben infolge Rezidivierung des Tumors.

RÉSUMÉ

L'auteur décrit et étudie le traitement des tumeurs malignes de l'oreille moyenne et de la mastoïde par l'opération radicale associée à l'irradiation par les rayons roentgen et le radium, sur une série de 12 cas. Cinq malades sont restés sans récidive pendant plus de 5 ans, un est mort sans signe de récidive deux ans et demi après l'opération, et six sont morts de récidive de la tumeur.

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VENOUS TRANSPORT OF Na^{22} FROM HEALING FRACTURES IN THE RABBIT TIBIA

by

LARS GÖTHMAN

KETY (1945, 1948, 1949) demonstrated that the disappearance of radioactive sodium injected locally into human gastrocnemius muscle is closely related to the regional circulation. Since then a number of investigations using this technique have been carried out and his results have been confirmed in studies on radiosodium disappearance in muscle (COOPER 1949; FRANKE, BOATMAN, GEORGE and MOSES 1950) and in subcutaneous tissue (FRANKE et coll.; DOUGLAS, CAMPBELL, MCINALLY and ROBERTSON 1952; RAGAPORT, SAUL, HYMAN and MORTON 1952). WALDER (1953, 1954, 1955) observed in perfusion studies using human and rabbit muscle that radiosodium disappearance, through its relation to the regional circulation, is a measure of the blood flow. PRENTICE, STAHL, DIAL and PONTERIO (1955) found that this relationship between radiosodium disappearance and the blood flow is linear in the biceps muscle of the dog, while ODEBLAD, NATI, SELIN and WESTIN (1956) established a relationship between these two factors when examining the circulation in the rabbit ovary. HÅSTAD, LARSSON and LINDHOLM (1959) demonstrated that there is a certain amount of agreement between the disappearance of radioactive sodium and the blood flow in the Achilles tendon in man.

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Only two reports seem to have been published on the disappearance of radioactivity from bone tissue. BRODIN (1955), in connection with studies on growth-promoting operations, attempted to determine the disappearance from a radioiodine deposit (I^{131}) in the bone marrow in a rabbit's tibia. He found, however, that the method was not sufficiently developed for this type of examination and that it gave no information on the local circulation. BERNASCHEK (1956), on the other hand, after a direct injection of I^{131} into the callus in 16-day-old fractures of the femur in rats, observed an increase in the blood flow in the fractures of animals treated with Padutin and Vasculat as compared with those of the controls. In both these investigations a scintillation counter was placed over the injected deposit.

The object of the present investigation was to measure the disappearance of a radiosodium deposit in the bone marrow and, with the assistance of this, to study the variations in the regional circulation in healing fractures in a rabbit's tibia and draw comparisons between the transport of the activity through the vessels of the tibia marrow and through vessels outside the tibia. The technique used diverged slightly from the conventional disappearance technique.

Material and Methods

Animals. The material in this report consists of 33 mature male and non-pregnant female rabbits, 6 of which (group I) were used for a study of the disappearance in an undamaged left tibia while the remaining 27 formed the fracture series (groups II to V). The weight of the animals varied from 2.2 to 3.5 kg.

Surgical technique. The animals were anaesthetized with 20 to 25 mg Nembutal per kg bodyweight administered intravenously, and with open drop ether. The operations were performed with sterile precautions. A small anteromedian incision was made in the middle of the left lower leg, and after extraperiosteal exposure of the tibia an oblique fracture was produced in it by sawing immediately below the synosteosis between the fibula and tibia. The fragments were placed in good position and firmly fixed with fine, stainless encircling wires. The wound was sutured with nylon thread and the entire hindleg was enclosed in a circular plaster cast.

Clinical and roentgenologic examination of the fractures. At the same time as the disappearance values were recorded a note was also made, after removal of the plaster cast, of the appearance of the wound on inspection, the size, shape, and solidity of the callus, and the stability of the fracture on palpation. A conventional roentgen examination of the lower leg, with views taken in two planes at right angles, was also carried out.

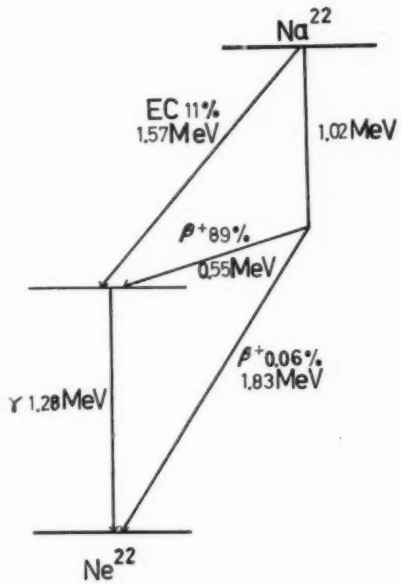


Fig. 1. Decay scheme of Na^{22}.

Isotope technique. The isotope used was Na^{22}, which is a β and γ emitter with γ energies amounting to 1.28 and 0.53 MeV (annihilation γ); its half-life is 2.6 years. The decay scheme of Na^{22} is shown in Fig. 1. The Na^{22} was used in the form of physiologic $Na^{22}Cl$ solution with a specific activity of approx. 2.4 μC/mg of Na.

After intravenous injection of 50 mg of heparin the animals were anaesthetized with 20 to 25 mg Nembutal per kg bodyweight administered intravenously, and with open drop ether. They were then bound so that the left leg was as far as possible in the same position in all experiments. The femoral vein was exposed through a small incision in the left groin, opened, and two of the arms of a triple-armed catheter of 1.1 mm calibre were inserted proximally and distally into it. The third, free arm was occluded with a clamp. The area where the nutrient vein leaves the nutrient canal of the tibia, on the lateral border of the tibia immediately above the synosteosis between the fibula and tibia, was exposed through a small incision on the lateral aspect of the lower leg, immediately above its middle segment. This incision was kept open with a small soft retractor. Through a tiny incision, approximately 1 cm above the ankle, the tibia was exposed medially and anteriorly and a hole was drilled through the corticalis with a 1.6 mm drill. The injection apparatus consisted of a needle (No. 20) inserted in a fine, 2 to 3 cm long, 0.4 mm polythene catheter that was introduced through the hole into the medullary cavity until the tip of the catheter was judged to be resting at the level of the central region of the fracture, or in the corresponding position in the medullary cavity of the undamaged tibia; 0.05 ml $Na^{22}Cl$ solution with an activity of 0.5 μC was then injected slowly and met with no appreciable resistance. Blood sampling was begun immediately after the conclusion of the injection, the exact time of the latter being carefully recorded. The samples were taken alternately from the femoral vein and from the nutrient vein during the first 25 minutes immediately following the injection. While the proximal arm of the triple-armed catheter in the femoral vein was shut off, the peripheral femoral blood was allowed to run out freely from the free arm into a glass bottle for exactly one minute. The blood samples from the nutrient vein were col-

lected by a technique described by ENGLUND (1956). The nutrient vein was cut at its outlet from its canal and the blood flowing out was sucked up with a small, triangular filter-paper, which was placed in a glass bottle as soon as it was thoroughly saturated with blood. The exact time required for saturation was determined; it varied from 20 to 74 seconds. After 1 ml of 0.1 normal hydrochloric acid had been added to each of the bottles, they were analyzed separately in a scintillation detector with standard geometry. After correction for the background the radioactivity (counts/min) per time unit (10^{-2} min) was calculated for the outflow in the individual blood samples. The values obtained for the disappearance of the radioactivity (expressed in counts/min$^2 \times 10^{-2}$) were plotted semilogarithmically with the radioactivity as the ordinate and the time after the injection of Na^{22} as the abscissa. A line for the values from the femoral vein and from the nutrient vein was drawn by hand and a determination for the disappearance constant, k, was thus obtained. According to KETY's formula (1948, 1949)

$$A = A_0 \cdot e^{-k \cdot t}$$

By derivation of this equation the following is obtained:

$$\frac{dA}{dt} = A_0 \cdot (-k) \cdot e^{-k \cdot t}$$

This means that (dA/dt), i. e. the disappearance of the radioactivity, decreases by the same k-value as A. Consequently it is possible to write:

$$k = \frac{log(dA/dt)_0 - log(dA/dt)_t}{0.434 \cdot t}$$

where dA/dt is the transport of activity in counts/min$^2 \times 10^{-2}$, and t is the time. In addition, the slope of the curve was also utilized to calculate the value for the transport of activity at the time *0*, by extrapolation. The value obtained for k denotes the fraction of activity that was carried away per minute. It is written as k_N for the nutrient vessels and as k_F for the femoral veins. The total disappearance is the sum of these two, i. e. $k_{tot} = k_N + k_F$. The k_{tot}-value corresponds to the result that is to be expected with the conventional disappearance technique. On account of technical difficulties in the experiments it was not possible to combine conventional disappearance measurements with the technique employed in this investigation.

Statistical method. There is reason to assume that both measurement errors and the biologic variation of k_N, k_F, and k_{tot}, as well as the extrapolated values, were normally distributed. As only a limited number of observations could be made there were reasons for using t-distribution in the estimation of the probability. Significance was considered to have been established if $p < 0.00$ (CRAMÉR 1949).

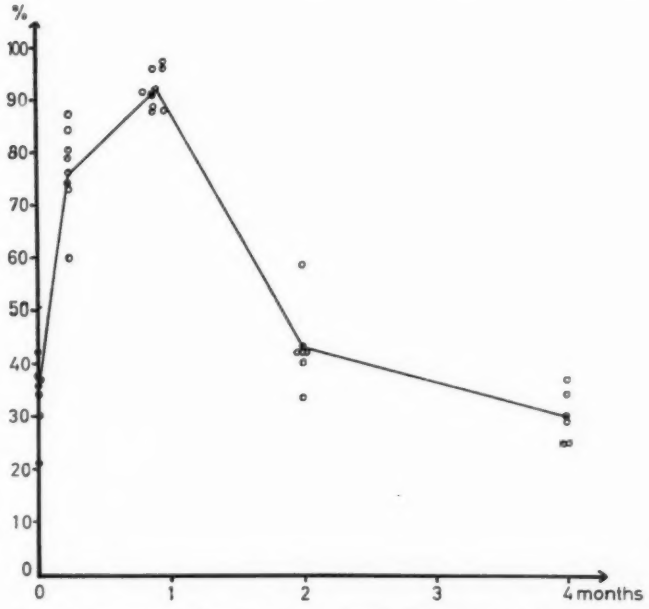


Fig. 2. Percentage of radioactivity (extrapolated to time *0*) transported through the femoral vein (F %) in groups I to V.

Results

Clinical and roentgenologic examinations. The 27 animals comprising the fracture series were divided according to the age of the fracture at the time of the disappearance tests into the following four groups:

Group II. One-week-old fractures, 7 animals. All wounds were without signs of infection. The fractures were slightly unsteady in a few instances but were firm in the others. They all had soft, rounded callus with indistinct borders and of moderate size; no callus was visible in the roentgen films. Good adaptation without angular deformity was observed.

Group III. Three to four-week-old fractures, 8 animals. All the wounds had healed by first intention and the fractures were almost completely rigid. The callus was now larger, more irregular, and much firmer. With the exception of one case with slight angulation, concave dorsally, none of the fractures showed displacement. A small amount of callus was visible in the roentgen films, mostly behind the fracture.

Table 1

The means and their standard errors for the percentage of radioactivity transported through the femoral vein (F %), the k-values for the femoral vein (k_F) and for the nutrient vein (k_N), and their sum (k_{tot}), in the different experimental groups. n = number of animals in each group.

Group	$F\ \%$ $M \pm \varepsilon_M$	k_F $M \pm \varepsilon_M$	k_N $M \pm \varepsilon_M$	k_{tot} $M \pm \varepsilon_M$	n
I.....	34 ± 3.0	0.150 ± 0.016	0.152 ± 0.012	0.302 ± 0.026	6
II	76 ± 8.4	0.058 ± 0.005	0.029 ± 0.005	0.087 ± 0.009	7
III.....	92 ± 1.3	0.274 ± 0.016	0.092 ± 0.007	0.366 ± 0.012	8
IV	43 ± 3.6	0.218 ± 0.012	0.227 ± 0.009	0.446 ± 0.017	6
V	30 ± 2.2	0.170 ± 0.009	0.208 ± 0.006	0.378 ± 0.013	6

Table 2

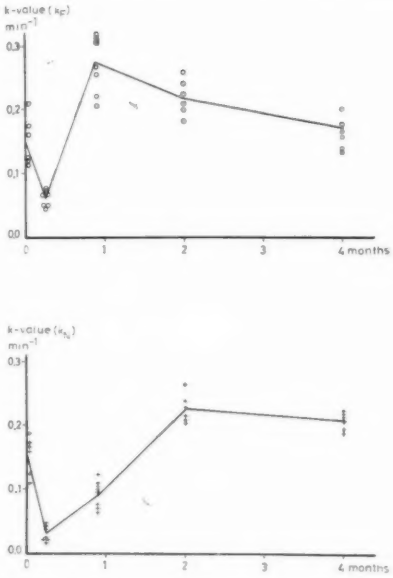
Differences between the various fracture groups (II to V) and group I with respect to the means of the percentage of radioactivity transported through the femoral vein (F %)

Groups	$M_D \pm \varepsilon_D$	M_D/ε_D	$n_1 + n_2 - 2$	Significance
II—I.....	+ 42 ± 4.4	9.5	11	Yes
III—I	+ 58 ± 3.3	17.6	12	Yes
IV—I	± 9 ± 4.7	1.9	10	No
V—I	− 4 ± 3.7	1.1	10	No

Group IV. Two-month-old fractures, 6 animals. All wounds had healed by first intention and all the fractures were firm. In general, spindle-shaped, fairly narrow callus, smooth and hard, with regular outlines, had formed. It was thickest dorsally and laterally and almost completely enclosed the fracture and to some extent the encircling wires, but the fracture lines had not entirely disappeared. There was no appreciable displacement.

Group V. Four-month-old fractures, 6 animals. The wounds were completely healed. No true callus could be palpated; there was possibly slight thickening of the tibia at the fracture site. All the fractures had healed without angular deformity. Only slight thickening or spindle-shaped enlargement at the site of the fractures was seen in the roentgen films; the fracture lines on the other hand had entirely disappeared.

Radiosodium disappearance measurements. The values obtained for the percentage of the radioactivity transported through the femoral vein ($F\ \%$), the disappearance constant for the femoral vein (k_F) and for the nutrient vein (k_N), and the sum of these constants (k_{tot}), are given in the diagrams in Figs 2 and 3.



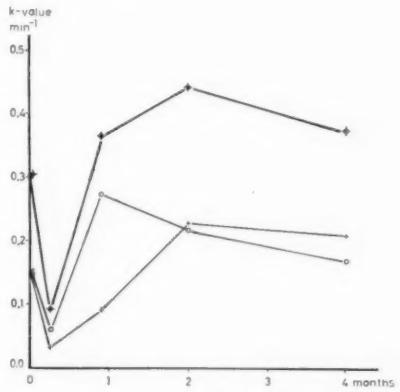


Fig. 3. Diagrams showing the k-values for the femoral vein (k_F) and the nutrient vein (k_N) in groups I to V (two diagrams to the left). In the diagram above the means of the k-values for the femoral vein (k_F) and for the nutrient vein (k_N) as well as for the sum of the k-values (k_{tot}) in groups I to V are given.

o mean for k_F, + for k_N, and ⊕ for k_{tot}.

Table 3

Differences between the various fracture groups and group I with respect to the means of the k_F-values

Groups	$M_D \pm \varepsilon_D$	M_D/ε_D	$n_1 + n_2 - 2$	Significance
II—I	-0.091 ± 0.017	5.4	11	Yes
III—I	$+0.124 \pm 0.022$	5.6	12	Yes
IV—I	$+0.068 \pm 0.019$	3.6	10	No
V—I	$+0.020 \pm 0.018$	1.1	10	No

in which the mean curves have also been plotted. The means for the above determinations for the different groups are also assembled in Table 1. As may be seen, the F % shows a considerable increase in group III, and then gradually decreases in groups IV and V to approximately normal values, in other words to the values obtained in undamaged bone (group I). After a reduction in group II, the k_F-values show a considerable increase in group III, followed by a gradual decrease in groups IV and V. The k_N-values also show a decrease, not only in group II but also in group III, while the values in groups IV and V are

Table 4

Differences between the various fracture groups and group I with respect to the means of the k_N-values

Groups	$M_D \pm \varepsilon_D$	M_D/ε_D	$n_1 + n_2 - 2$	Significance
II—I	-0.123 ± 0.013	9.5	11	Yes
III—I	-0.060 ± 0.014	4.3	12	No
IV—I	$+0.008 \pm 0.015$	5.0	10	Yes
V—I	$+0.056 \pm 0.013$	4.3	10	No

Table 5

Differences between the various fracture groups and group I with respect to the means of the k_{tot}-values

Groups	$M_D \pm \varepsilon_D$	M_D/ε_D	$n_1 + n_2 - 2$	Significance
II—I	-0.215 ± 0.027	7.9	11	Yes
III—I	$+0.064 \pm 0.028$	2.3	12	No
IV—I	$+0.144 \pm 0.031$	4.6	10	Yes
V—I	$+0.076 \pm 0.029$	2.6	10	No

Table 6

Differences between the means of the k_F and k_N values in each group

Group	$M_D \pm \varepsilon_D$	M_D/ε_D	$n_1 + n_2 - 2$	Significance
I.....	-0.002 ± 0.020	0.1	10	No
II	$+0.029 \pm 0.007$	3.9	12	No
III.....	$+0.182 \pm 0.017$	10.7	14	Yes
IV	-0.009 ± 0.014	0.7	10	No
V	-0.038 ± 0.011	3.5	10	No

approximately the same as those for k_F. As regards the sum of the disappearance constants (k_{tot}), this shows a sharp reduction in group II but increases in the other fracture groups, especially in group IV.

Comparing the individual fracture groups with the control from the standpoint of the percentage of the radioactivity transported through the femoral vein ($F\,\%$) a significant decrease is noted in group II and a sharp increase in group III, while in the other groups no differences from group I are observable (Table 2).

The differences between the means of the k_F-values in the fracture groups and in group I are shown in Table 3. A significant decrease is observed for

group II and a significant increase for group III. Table 4 demonstrates the corresponding differences for the k_N-values; these also show a strong decrease for group II, and a less marked, though significant, increase for group IV.

In Table 5 will be found the differences between the means of the sums of the k_F- and k_N-values (k_{tot}). These show a significant decrease in group II and a significant increase in group IV as compared with group I.

The differences between the means of the k_F-values and k_N-values in each group appear in Table 6. Only in group III is there a significant difference; the k_F-values in this group are much higher than the k_N-values.

Discussion and Conclusions

The venous anatomy of the rabbit tibia has been described by a number of authors. The majority (HASHIMOTO 1935, DE MARNEFFE 1951, ECOIFFIÉ, PROT, GRIFFIE and CATACH 1957, BROOKES and HARRISON 1957, BRÅNEMARK 1959) considered that in general the larger veins follow the course of the arteries, in other words that there is one main vein in the medullary cavity, the nutrient vein, which is formed through the union of a proximal and a distal tributary. This vein emerges through the nutrient canal. The aforementioned investigators are, however, of the opinion that there are two or three other medium-sized veins in the metaphyses which pass out through the metaphyseal cortex to the large veins in the soft tissues at the knee and ankle joints. These metaphyseal veins, which are believed to be more numerous in the upper metaphysis than in the lower, anastomose with the main vein through communications in the medullary cavity. BROOKES and HARRISON, as well as BRÅNEMARK, stated that there is also an emissary vein, which issues from and is a smaller branch of the distal stem of the nutrient vein and empties through an opening in the lateral cortex approximately 1.5 cm below the synosteosis between the fibula and tibia. MORGAN (1959), on the other hand, considered that the emissary vein is the main vein of the tibia marrow and that no equivalent to the nutrient vein exists. The conclusion to be drawn from this is that when radioactivity is deposited in the medullary cavity in the middle of the diaphysis, that portion of the activity which is carried away by the veins of the medullary cavity is probably mostly transported through the nutrient vein. Sources of error may, however, arise through the fact that a small amount of activity is transported through the aforementioned metaphyseal veins anastomosing with the nutrient vein in the medullary cavity; these veins, in their turn, empty through the larger soft tissue veins into the femoral vein. However, the present author considered that these sources of error were small in this investigation, and that as regards the middle of the diaphysis the nutrient vein may be taken to be a representative pathway for the veins of the medullary cavity.

It will be seen from the diagram in Fig. 4, which shows an example from a radiosodium disappearance measurement, that the values plotted for the ac-

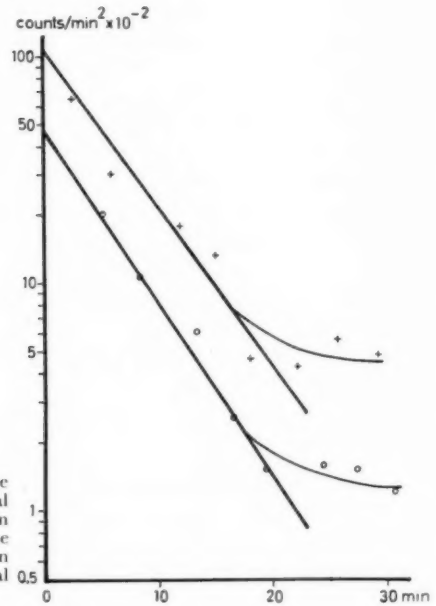


Fig. 4. Example of a radiosodium disappearance measurement. Disappearance curve for the femoral vein (o—o—o—o), and for the nutrient vein (+—+—+—+). Extrapolated activity for the femoral vein 47 (30 %) and for the nutrient vein 110 counts/min^2 × 10^{-2}. *k*-value for the femoral vein 0.174 and for the nutrient vein 0.158.

tivities cleared through the femoral vein and through the nutrient vein form straight lines for the period corresponding to the first 15 to 20 minutes after the deposition of the radiosodium in the medullary cavity whereas for the later part of the experiment they diverge from a straight line to form a sloping curve. There may be several reasons for this deviation, which was noted in nearly all the experiments. A small amount of the injected deposit may spread by diffusion to poorly vascularized tissues situated fairly far out in the surrounding areas, and thus may produce a slower, delayed phase in the clearance of the radioactivity. The trauma caused by the blood sampling process may be another explanation. WALDER (1953) and ENGLUND (1956) have previously demonstrated that irritation of the vessels in the vicinity of a deposit caused a circulatory disturbance which manifested itself in the disappearance curves as a divergence from a straight line. In the present investigation it is conceivable that both the catheter in the femoral vein and the trauma to the nutrient vein in association with the absorption of blood with the filter-paper constituted irritation injuries to these vessels and produced the change observed in the disappearance curves. In most of the experiments, the deviation from a straight line was most marked in the curve for the nutrient vein. It may be pointed out that the repeated traumata to which this vessel was subjected were na-

urally greater than the injury suffered by the femoral vein in connection with the presence of the catheter. The radioactivity circulating in the blood is a third possible explanation of the deviation noted; this activity ought to increase towards the end of the experiment. In six experiments a sample was taken from an ear vein immediately after the blood sampling from the femoral and nutrient veins had been concluded (i. e. about 25 minutes after injection of the radiosodium deposit); analysis of these samples gave activity values varying from 81 to 319 counts/min per gram of dried blood (mean 177). Admittedly, these values are very low but they may have contributed in some measure towards delaying the activity.

The investigation revealed that radioactivity deposited in the medullary cavity of the tibia was carried away through the femoral vein to a higher degree in 3 to 4-week-old fractures than in undamaged bone. This suggests that there is increased vascularity in the soft parts outside the tibia during this phase of active callus formation, a supposition that accords well with the findings reported by BELLMAN, GÖTHMAN, ODÉN, STRÖMBECK and VELANDER (1956) and by GÖTHMAN (1959, 1960). In the last-named microangiographic investigations (1960) into the vascularization of experimental fractures in the rabbit tibia, a considerable increase in newly formed blood vessels radiating in towards the fracture from adjoining soft tissues was observed, especially in 2 to 3-week-old fractures, while the corresponding vascular reaction in the medullary cavity was much less marked.

The *k*-values for the femoral vein also showed a considerable increase in the 3 to 4-week-old fracture group, not only when this group was compared with the control group but also as compared with the *k*-values for the nutrient vein in the fracture group in question. This suggests that there was an increase in the local circulation within the region where the vessels empty through the femoral vein, i. e. the soft tissues outside the tibia, at this stage of the callus formation. The *k*-values for the nutrient vein, on the other hand, did not increase until later in the healing process, in other words in the 2-month-old fractures. The same feature was observed with regard to the sum of the *k*-values; this indicates that the increase in the regional circulation in the medullary cavity reached its maximum later than that in the soft tissues outside the bone. At the time when clinical and roentgenologic healing of the fracture was established (4 months), no significant difference was noted for the *k*-values or for the amount of activity removed as compared with group I.

As regards group II (one-week-old fractures), significant differences were established both for the amount of activity transported off and for the *k*-values, but as the absolute figures were in all cases very small in this group as compared with the other groups no definite conclusions can be drawn. In these recent fractures, the radioactivity was deposited in the centre of a haematoma, in which presumably the diffusion pathways are so long that the activity cannot conceivably reach the capillaries within a reasonable time. ODEBLAD,

WESTIN and ENGLUND (1959) have demonstrated (in equation 9) that the k-value decreases with an increased diffusion pathway.

Appendix

ε_D : Standard error of a difference $\varepsilon_D = \pm \sqrt{(\varepsilon_{M_1})^2 + (\varepsilon_{M_2})^2}$

ε_M : Standard error of a mean $\varepsilon_M = \pm \frac{\sigma}{\sqrt{n}}$

$F\,\%$: Percentage of radioactivity transported through the femoral vein at time θ

k_F : Disappearance constant for the femoral vein

k_N : Disappearance constant for the nutrient vein

k_{tot} : $k_F + k_N$

M : Arithmetic mean $M = \frac{\Sigma x}{n}$

M_D : Difference between two arithmetic means

n : Number of experimental animals

σ : Standard deviation $\sigma = \pm \sqrt{\frac{\Sigma (x - M)^2}{n - 1}}$

x : Individual observation in a statistical distribution.

SUMMARY

The venous transport of Na^{22} injected into the medullary cavity of undamaged and fractured tibias, has been studied in 33 rabbits. The radioactivity was determined in samples of venous blood obtained from the femoral vein and from the nutrient vein, both the k-value (disappearance constant), measured by a modification of KETY's formula, and the percentage of transported radioactivity being ascertained for each of the two outflow pathways. The results suggest that an increase in the regional circulation outside the tibia takes place in 3 to 4-week-old fractures and that the circulation in the medullary cavity increases at a later stage in the healing process.

ZUSAMMENFASSUNG

Es wurde der venöse Transport von Na^{22}, das in die Markhöhle von intakten und frakturierten Schienbeinen injiciert worden war, an 33 Kaninchen untersucht. Die Radioaktivität wurde aus Proben venösen Blutes von der femoral- und einer nutritiven Vene bestimmt und sowohl der k-Wert ('disappearance' Konstante), gemessen nach einer Modifikation der Formel nach KETY, als auch der prozentuelle Anteil von transportierter Radioaktivität für beide Abflusswege bestimmt. Die Ergebnisse lassen vermuten, dass eine Steigerung der regionalen Zirkulation ausserhalb des Schienbeines bei 3 bis 4 Wochen alten Frakturen stattfindet und dass sich die Blutzirkulation in der Markhöhle erst in einer späteren Phase des Heilungsverlaufes erhöht.

RÉSUMÉ

L'auteur a étudié sur 33 lapins le transport veineuse de Na^{22} injecté dans la cavité médullaire de tibias intacts et fracturés. La radioactivité a été mesuré sur des échantillons de sang provenant de la veine fémorale et de la veine nourricière. La valeur de k (constante de disparition), mesurée par une modification de la formule de KETY, et le pourcentage de radioac

tivité transportée ont été déterminés pour chacune des deux voies efférentes. Les résultats de ces mesures font penser qu'il se produit une augmentation de la circulation régionale en dehors du tibia dans les fractures datant de 3 à 4 semaines et que la circulation dans la cavité médullaire augmente à un stade plus tardif du processus de guérison.

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FROM THE INSTITUTE OF RADIOPHYSICS (DIRECTOR: PROF. R. M. SIEVERT), KING GUSTAV V JUBILEE CLINIC, KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN.

A HIGH-VOLTAGE AND RAY-PROOF ROENTGEN EQUIPMENT FOR IRRADIATION OF SMALL AND MEDIUM-SIZED OBJECTS

by

R. THORAEUS

Irradiation of small and medium sized objects, for example animals, is frequently carried out in routine investigations and in research. Adequate precautions must always be taken to avoid hazards to the personnel engaged, which means that the radiation must be effectively absorbed in all directions.

The tube in its container is usually suspended from the ceiling or fixed to a wall and located in a room separated from the remainder of the plant. The room must be provided with adequate protection in the walls, ceiling and floor. The switch-table must be placed outside the room and behind an inspection window of lead glass. All these arrangements are expensive, and require considerable space of which most laboratories are short.

From earlier experience of shock-proof and ray-proof roentgen tube containers (3) and of an installation with complete protection installed at the beginning of 1952, improved equipment was designed about three years ago for use at Radiumhemmet. This unit is now briefly described.

The equipment is illustrated in Fig. 1 and consists of two main parts, viz. the roentgen tube and its shock-proof and ray-proof container, and the 'irradiation room' which is completely enclosed and protected. The tube and container are of the type described in detail in a previous paper (3), to which the reader is referred. It may be stated here that the container may be used with tube voltages up to 200 kV constant potential and with tubes of differ-

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ent makes. With an ordinary thin-walled 200 kV therapy tube, the inherent filtration of the unit is usually equivalent to 1 to 1.5 mm Al. This favourable condition makes it possible to operate at tube voltages between 50 and 200 kV and with a correspondingly wide range of radiation qualities. The oil cooling system enables the maximum rating of the tubes, usually up to 15 or 20 mA, to be employed; at 195 kV constant potential radiations of up to 2 mm Cu HVL may be obtained.

The 'irradiation room' consists of a lead-lined wooden box (B) resting on a horizontal frame (A) provided with four supports (S_2); the size of the box and supports are given in the figure. The roentgen tube and its container (C) is positioned on two supports (S_1) at the top of the box. The roentgen tube is connected to the high voltage generator by flexible rubber-insulated cables.

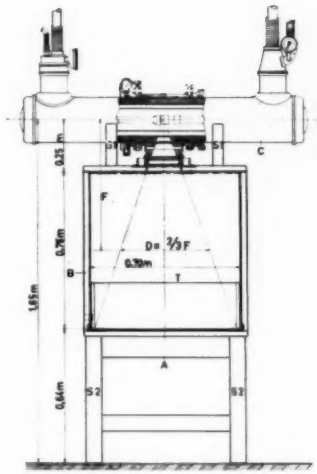

Fig. 1. Vertical section of the equipment installed at Radiumhemmet.

The lead protection of the box is sufficient for tube voltages up to 250 kV. The geometry of the equipment is such that the primary radiation, even at the maximum width of the beam, can reach only the bottom of the box, as shown in the figure. This means that only the bottom needs to be provided with protection against the primary beam; the vertical sides and the top require protection only for secondary radiation. Due to this effective utilization of the protection material the weight of the lead-lined box with supports, but without the roentgen tube and its container, is not more than about 270 kg; the weight of the container and tube is about 150 kg, a figure that can be somewhat reduced by using an oil-insulated container although only one type of tube can then be used with that particular container.

There is a table (T) of plywood in the lead-lined box which can be positioned at focal distances of from 25 to 100 cm. The maximum available diameter of the irradiated field on the table is about two-thirds of the focal distance. If desired this diameter may be reduced by employing a smaller diaphragm; the container is supplied with three extra diaphragms by which the diameter of the beam can be reduced to three-quarters, a half, and a quarter of the maximum. Concentric circles are drawn on the upper side of the table to indicate the maximum field sizes at frequently used focal distances. The beam enters the box through an opening at the top, the diameter of which corresponds to the maximum width of the beam. A vertical lead collar is ar-

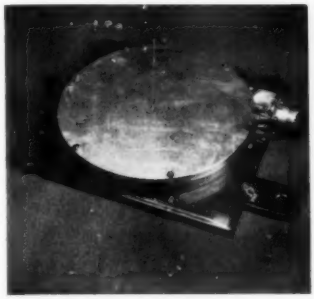

Fig. 2. Monitoring filter fitting the type of tube container used.

ranged around this opening to absorb secondary radiation from the filter, diaphragm, etc.

The box may be provided with inspection windows of lead glass, and suitable illumination of the interior may also be arranged. One of the vertical sides of the box is designed to constitute a door, but more than one door may be obtained if necessary. The door is provided with an automatic switch so arranged that the roentgen tube cannot be operated as long as the door remains unfastened. If the box is fitted with more than one door, each should be provided with a switch and the switches connected in series.

The air volume of the box is nearly 400 litres which may be sufficient for an exposure of at least 20 minutes when a small or medium sized animal is being irradiated. In addition, the air is slightly heated by the animal, and this in turn will cause some air exchange through the opening at the top of the box and extend the exposure time. Using a focal distance of 35 cm, maximum field size (23 cm in diameter), 175 kV, and a moderate filtration giving a HVL of about 1 mm Cu, an exposure dose rate of about 100 r/min is easily obtained (see also Table). Under these conditions an exposure of 20 minutes corresponds to about 2 000 r. If air is slowly forced into the box, or drawn from it by a fan, the question of any limitation of the exposure by the ventilation need not be considered.

Operation conditions of 195 kV constant potential and 15 mA mean a continuous discharge of 2.9 kilowatts. The dissipation of the corresponding amount of heat from the anode requires an effective and ample cooling system, for which purpose a cooling pump of the type previously described (4) is used. The cooling medium used in the anode system is a non-conducting oil that in turn is re-cooled in the pump unit by tap-water. Using an oil flow of about 17 litres per minute, and a water flow of about 8 litres per minute, a continuous discharge of 3 kilowatts is possible with oil temperatures below 40° C, which is well within the safety range. The great advantage of using non-conducting cooling media in roentgen technique was considered as early as 1928, and led to the first unit of this system which was installed in the

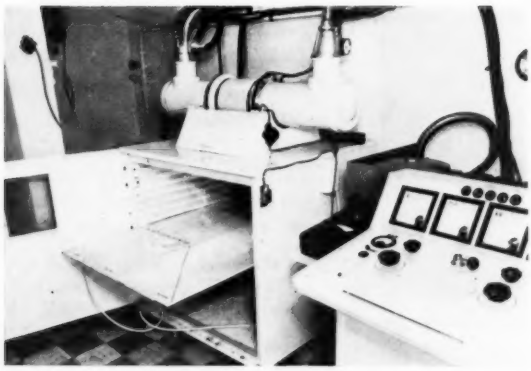

Fig. 3. Photograph of the apparatus installed at the Institute of Tumour Biology (published by courtesy of the institute).

roentgen therapy department of Radiumhemmet at the beginning of 1929; a photograph and a description of its principle were given in a previous paper (2). Since then the use of non-conducting cooling media has considerably increased and is nowadays universal in modern roentgen therapy apparatus.

The high voltage generator required to operate the roentgen tube may be of any type and make. The terminals of the tube and generator are connected by shock-proof cables, so that the generator may be located some distance away, or in a separate space, if desired. Constant potential generators are preferred because of their high efficiency in both dose rate and HVL of radiation. Enclosure of the generator in one or two oil-filled tanks is also preferred because of the smaller space then required; such a generator may be placed near the tube container, the cables then being quite short. The switch-table of the generator may be positioned where required. As a matter of fact the complete equipment will not occupy a floor area of more than a few square meters.

To obtain a reliable determination of the radiation output from a roentgen tube, as well as of its stability, the use of monitoring filters, as previously described (5), have proved both convenient and effective. Fig. 2 shows such a filter. Its filtration corresponds to 0.5 Cu + 1 Al, and the design is arranged to fit the type of tube container employed. By changing the distribution of the filter plates on the two sides of the air volume enclosed, the response of ionization current in a monitoring filter may be changed considerably; a ratio 1 : 3 is easily attainable with filters of 0.5 Cu or more. If an extra high response is desired, the walls of the chamber are made of 0.5 mm Al with thin Al foil as the inner electrode. Such a monitor has the mechanical strength required and its filtration is equivalent to 1 mm Al which constitutes the basic added filter to be supplemented with further filters as required.

If the monitor is connected to a current-measuring instrument (galvanometer, microammeter, etc) in the switch-table, the stability of the radiation output from the tube may be watched. It is also easy to position a direct reading, integrating instrument in the switch-table, and to connect this instrument to, either a monitoring filter, thus integrating the air dose from the tube, or to a suitably sized thimble chamber by which the dose received by the object can be integrated. Doses up to 10 000 r can be measured at a single integration by means of the latter arrangement.

The radiation dose received by the object may also be measured by condenser dosemeters. An adequate number of the miniature condenser dosemeters designed by SIEVERT (1) are particularly convenient for this purpose; with a sufficient number of such dosemeters the required survey of the radiation received, and its distribution over the object irradiated, may be obtained at a single exposure.

Information on the qualitative and quantitative properties of the beam obtained with the present apparatus may be of interest. Some measurements of the half-value layer in millimeters of copper, and of the exposure dose rate in r per minute free in air in the lead-lined box, at 35 cm focal distance, maximum field diameter, 15 mA, with selected combinations of tube voltage and added filtration have therefore been made and are collected in the Table below.

Table

Tube voltage kV	Added filter	HVL mm Cu	Exposure dose rate in r/min free in air at 35 cm focal distance, maximum field diameter of 23 cm and 15 mA
100	1 Al	0.1	86
140	4 Al	0.3	109
195	4 Al	0.6	215
195	0.5 Cu + 1 Al	1	143
195	Thoraeus-filter	2	74

It is evident that the type of equipment described has considerable flexibility, and a good output efficiency. It is very economical and may be modified as required for any special purpose. Fig. 3 shows another unit of the same type recently installed at the Institute of Tumour Biology of Karolinska Institutet. This is a compact, wellplanned and effective unit, into which many of the facilities mentioned above have been incorporated, e. g. a lead glass window in the door and an integrating dosemeter. An automatic ventilation of the box is obtained by utilizing the ventilation of the tube container. The high voltage generator and the switch-table lie to the right of the irradiation unit. A unit of the same type as shown in Fig. 1 was also recently installed in the radiobiology section of the Institute of Radiophysics.

SUMMARY

A compact high-voltage and ray-proof apparatus for the roentgen irradiation of small and medium-sized objects such as animals is described.

ZUSAMMENFASSUNG

Eine kompakte und strahlensichere Hochspannungsanlage für Röntgenbestrahlung von kleinen und mittelgrossen Objekten, wie z. B. Tieren, wird beschrieben.

RÉSUMÉ

L'auteur décrit un appareil peu encombrant, fonctionnant sous une tension élevée, protégé, destiné à l'irradiation roentgen d'objets de dimensions petites et moyennes tels que des animaux d'expérimentation.

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AUS DER RÖNTGENABTEILUNG (LEITER: PROF. L. DIETHELM) DER CHIRURGISCHEN UNIVERSITÄTSKLINIK KIEL (DIREKTOR: PROF. R. WANKE), DER CHIRURGISCHEN ABTEILUNG DER STÄDTISCHEN KRANKENANSTALTEN OLDENBURG (CHEFARZT: DOZENT W. LENTZ) UND DER TECHNISCH-WISSENSCHAFTLICHEN ABTEILUNG DER C. H. F. MÜLLER A. G., HAMBURG, DEUTSCHLAND.

STRAHLENGEFÄHRDUNG BEIM GEBRAUCH TRANSPORTABLER BILDVERSTÄRKER

von

L. DIETHELM, G. JÖTTEN, W. LENTZ und L. VÖLKEL

Diese Arbeit enthält Bemerkungen zur gleichnamigen Arbeit von KOCKUM, LIDÉN und NORMAN.

Die Verfasser haben an dem BV-Durchleuchtungsgerät, Müller BV-20, u. a. physikalische Strahlenschutzmessungen durchgeführt. Die Versuchsanordnung entspricht nicht bei allen Messungen den Einstellungen und Anforderungen, wie sie in der Praxis üblich sind. Nur bei Einhaltung praxisnaher Bedingungen ergeben Phantomprüfungen eine recht gute Vergleichsmöglichkeit für die in der Praxis zu erwartenden Werte. Aus diesem Grunde sehen wir uns veranlaßt, zu der Arbeit von KOCKUM, LIDÉN und NORMAN Stellung zu nehmen.

Wie bei allen röntgenologischen Untersuchungen ist auch bei der BV-Durchleuchtung die Röhrenspannung und die Röhrenstromstärke dem zu durchstrahlenden Objekt anzupassen und ein bestimmter Objekt-Fokus-Mindestabstand einzuhalten. Normalerweise findet für den BV-20 ein Durchleuchtungstubus Verwendung, der die Einhaltung eines Fokus-Haut-Abstandes von 35 cm gewährleistet. Bei den in Lund durchgeführten Messungen wurde jedoch der kürzere Tubus verwendet, der nur für die Fälle bestimmt war, in denen Durchleuchtungen an sperrigen Lagerungstischen aus Mangel an Beweglichkeit des Bildverstärker-Statives sonst nicht möglich sind. Seitdem das für die Anwendung des BV-20 entwickelte Extensionsgerät Maquet BV-6090 zur Verfügung steht, wird auf die Verwendung des kurzen Tubusses verzichtet. Es erscheint daher sinnvoll, den Strahlenschutz des BV-20 nur in Verbindung mit dem üblichen 35 cm Tubus zu prüfen.

Unter Bedingungen, die der Praxis für die Durchleuchtung eines Unterschenkels (Abb. 1) und eines Oberschenkels (Abb. 2) oder eines Schenkelhalses im dorsoventralen Strahlengang gerecht werden, wurden von uns Strahlenschutzmessungen vorgenommen und die Ergebnisse in den Abb. 1 und 2 graphisch dargestellt. Für diese Messungen wurde aus dem Laboratorium der C. H. F. Müller A. G., Hamburg ein Dosimeter mit Ionisationskammern (eigene Fertigung) benutzt, deren Wellenlängenabhängigkeit im Spannungsbereich von 50—100 kV (HWS 1.5 bis 4.0 Al) $\pm$ 5 % beträgt.

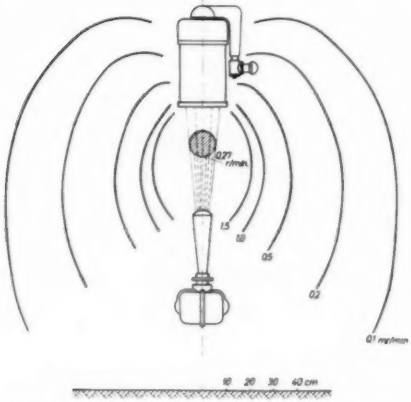

Abb. 1. BV-20-Oberflächen und Streustrahlen-Dosisleistungen. Durchleuchtung 55kV, 1 mA, 3.5 mm Al-Filter. Wachsphantom 11 cm diam., 45 cm Länge. Fokus-Phantom-Abstand 60 cm.

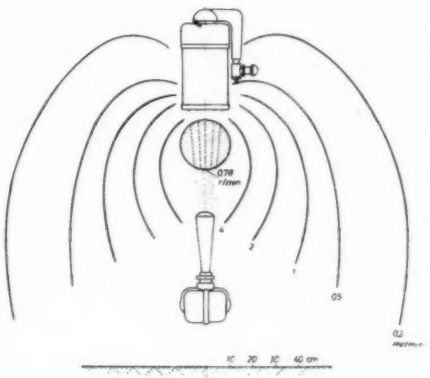

Abb. 2. BV-20-Oberflächen und Streustrahlen-Dosisleistungen. Durchleuchtung 75 kV, 1 mA, 3.5 mm Al-Filter. Wachsphantom 22 cm diam., 45 cm Länge. Fokus-Phantom-Abstand 55 cm.

Wie aus Abb. 1 ersichtlich, ergibt sich für das Unterschenkel-Phantom an der Oberfläche im Zentralstrahl eine Dosisleistung (Dosisleistung frei Luft einschließlich Rückstreuung) von 0.27 r/min und für das Oberschenkel-Phantom entsprechend Abb. 2 eine solche von 0.78 r/min. Diese Werte entsprechen der Hautbelastung des Patienten und gelten gleichfalls für die Strahlenbelastung einer ungeschützten Hand, die beispielsweise beim Reponieren von ungeschwächter Primärstrahlung getroffen wird.

Das Röntgenstrahlenbündel ist auf das Eintrittsfenster der BV-Röhre exakt eingeblendet; es wird nur das nutzbare Feld des primären Leuchtschirmes der BV-Röhre ausgeleuchtet. Jedes Hineinfassen der Hände in den primären Strahlenkegel wird vom Beobachter wahrgenommen. Da es sich beim Einrichten einer Fraktur nicht vermeiden läßt, daß der Repositeur mit seinen Händen in die ungeschwächte Nutzstrahlung hineingreift, ist für ihn das Tragen von Schutzhandschuhen unerläßlich. Leichte Schutzhandschuhe mit einem Bleigleichwert von 0.2 mm sind zu solchen Arbeiten flexibel genug und ermöglichen ein sicheres Reponieren.

Untersuchungen von Glocker und Zieler über die Schutzwirkung von Bleigummihandschuhen haben ergeben, daß solche mit 0.2 mm Bleigleichwert eine mit 3.5 Al vorgefilterte Primärstrahlung (Pulsierende Spannung) von 55 kV um einen Faktor 50 und eine Röntgenstrahlung von 75 kV entsprechend gleicher Vorfilterung um einen Faktor 16 schwächen. Dies würde beispielsweise bedeuten, daß bei einer Unterschenkel-Reposition, die unter Durchleuchtungsbedingungen gemäß Abb. 1 erfolgt, die Hände des Repositeurs beim Tragen solcher leichten Bleigummi-Handschuhe einer Strahlenbelastung von etwa 5 mr/min und unter Bedingungen der Abb. 2 einer Strahlenbelastung von ca. 50 mr/min ausgesetzt sind.

Unter Berücksichtigung der Empfehlungen der Internationalen Strahlenschutzkommission ergeben sich als höchstzulässige Durchleuchtungszeiten pro Woche dann für die Hände des Repositeurs bei Verwendung von Bleigummi-Handschuhen gemäß Abb. 1 300 min und gemäß Abb. 2 30 min. Die Praxis hat gezeigt, daß diese Grenzwerte nie erreicht werden und Durchleuchtungsdaten von 75 kV bei 3 mA nur für die Durchleuchtung des Schenkelhalses in transversaler Richtung erforderlich sind. Auf das Tragen von Schutzhandschuhen kann hierbei jedoch verzichtet werden, da eine Reposition von Hand nicht erfolgt.

Um die räumliche Verteilung der Streustrahlung übersichtlich darzustellen, wurden unsere Meßergebnisse in einem Polar-Koordinatensystem eingetragen. Die Abbildung 1 läßt erkennen, daß seitlich vom Zentralstrahl — in einer Entfernung von 20 cm etwas unterhalb des Phantoms — die Streustrahlen-Dosisleistung etwa 1.5 mr/min und in Abbildung 2 etwa 4 mr/min beträgt. Demnach könnte also ein Beobachter unter Bedingungen der Abbildung 1 200 min oder entsprechend Abbildung 2 etwa 75 min durchleuchten. Dennoch wäre es wünschenswert, leichte Schutzschürzen zu tragen. Bei horizontalem bzw. transversalem Strahlengang für die Schenkelhalsdurchleuchtung liegen die Verhältnisse günstiger, da Operateur oder Beobachter vom Objekt selbst gegen Streustrahlung abgeschirmt werden. Bei allen diesen Eingriffen sollte man bestrebt sein, nicht durch zu helles Licht oder direktes Sonnenlicht die Röntgenstrahlenintensität unnütz zu steigern. Dies geht auf Kosten des Strahlenschutzes.

In Deutschland gelten für den Hersteller bestimmte Mindestanforderungen an die Beschaffenheit medizinischer Röntgen-Anlagen und Einrichtungen, die in der Norm DIN 6811 festgelegt sind. Die Norm fordert unter anderem, daß für Röhrenschutzgehäuse die Dosisleistung bei Nennspannung und Dauernennstrom 20 μr/s in 1 m Abstand vom Brennfleck außerhalb des maximalen Nutzstrahlenkegels nirgends überschritten werden darf. Diese Forderung ist beim Röhrenschutzgehäuse des BV-20 erfüllt, und es spricht auch nicht dagegen, wenn um das Röhrenschutzgehäuse gelegte Filme belichtet werden. Die aus dem Röhrenschutzgehäuse noch außerhalb des Nutzstrahlenbündels austretende Strahlung ist in den Isodosisleistungskurven unserer Abbildungen 1 und 2 mit erfaßt. Ein Vergleich unserer Meßergebnisse mit denen aus obiger Arbeit ist nur bei Abbildung 1c) möglich, wobei zu berücksichtigen ist, daß in Lund bei dreifachem Röhrenstrom gemessen wurde. Unter dieser Voraussetzung liegt praktisch eine Übereinstimmung beider Meßergebnisse vor, wenn man in Betracht zieht, daß Streustrahlen-Messungen bei nicht eindeutig definierten Raumverhältnissen unter sonst gleichen Bedingungen durch den Einfluß von Tertiärstrahlung recht unterschiedlich ausfallen können. Auf die weiteren Meßergebnisse einzugehen, erübrigt sich, da bei den gewählten Bedingungen der Abbildung 1a, 1 b, 1 d, 1 e und 1 f kein brauchbares Durchleuchtungsbild zu erzielen ist.

Die Arbeitstechnik mit einem Bildverstärker ermöglicht zwar eine Beschränkung der Durchleuchtungszeit je Woche gegenüber konventionellen Durchleuchtungseinrichtungen, doch wie bei allen Untersuchungsgeräten bleibt aber nur bei sinnvollem und zweckentsprechendem Arbeiten die Strahlenbelastung für den Arzt weit genug von der Gefahrengrenze entfernt. Gegebenenfalls müßte man bei bestimmten Durchleuchtungseinstellungen an diesem Gerät durch Tragen leichter Schutzkleidung für den erforderlichen Strahlenschutz sorgen. Bei Einhaltung dieser Vorsichtsmaßnahmen können die Vorteile dieser BV-Einrichtungen für den praktischen Betrieb voll wahrgenommen werden.

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RADIATION HAZARDS ATTENDING THE USE OF TRANSPORTABLE IMAGE INTENSIFIERS

by

J. KOCKUM, K. LIDÉN and O. NORMAN

We have had an opportunity of reading the previous article by DIETHELM et coll. through the courtesy of the Editor of Acta Radiologica.

It is difficult for us to understand why these authors have found it necessary to make these objections since any major difference in opinion which may be conveyed does not in point of fact exist. Thus both the present writers and DIETHELM et coll. agree: that the apparatus is a roentgen apparatus and has to be treated as such and the usual protective measures are necessary; that one must naturally try to work with the object as close as possible to the intensifier; that only through the appropriate handling of the apparatus can full use of this valuable contribution to the roentgenologic arsenal be ensured. Furthermore the results of our measurements have not been seriously challenged and still give a reasonably correct overall picture of 'die Strahlengefährdung beim Gebrauch transportabler Bildverstärker' (the radiation hazards attending the use of transportable image intensifiers) under the given conditions.

DIETHELM et coll. state, however, that in some cases the experimental arrangement does not correspond to the routine handling of the apparatus in practice. They protest that our measurements were performed not only at the optimal position of the object, close to the amplifier, but also near the roentgen tube at the end of a short cone.

It is apparent from the literature, and we know from our own experience, that the handling of the apparatus varies considerably in practice. A complete assessment of the radiation hazards around a given roentgen apparatus cannot consequently be made merely by a study of the conditions at an optimal position. It is necessary that the maximal risk as well as the minimal risk should be investigated. Our observation points were selected as extreme positions in order to examine the entire region within which the hazards may vary. From measurements in these positions it is possible, at least approximately, to estimate the dose data in the intervening

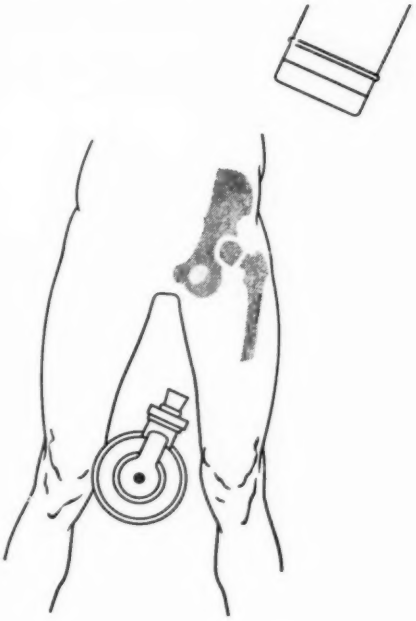

Fig. 1. Abb. 9 from reference (3).

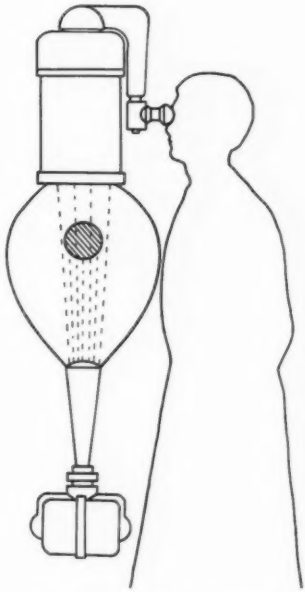

Fig. 2. Abb. 3 from reference (1).

locations corresponding to the various positions of an object in practice. We dare say that this is not possible from the data obtained from the measurements of DIETHELM et coll. in their last paper (2).

DIETHELM's et coll. description of the method of their own measurements is doubtlessly meant as constructive criticism. They have placed the phantom in the optimal position of the object to be investigated, close to the intensifier, i. e. in the same way as in our Fig. 1a, b, c. However, in spite of this they approve only our arrangement as shown in Fig. 1c. This is especially surprising as they themselves published measurements in 1956 (1), where the dose data are given for a FSD of 35 cm, i. e. close to the end of the longer cone. With these earlier measurements, the authors themselves illustrated the hazards at an unfavourable position of an object and according to them such a position is common in practice. They now criticize the fact that we, as a logical consequence, extended the measurements to the most unfavourable position, i. e. with the object close to the short cone. We would like to point out, however, that the short cone used to be delivered with the roentgen equipment and that it was sometimes used by DIETHELM et coll. themselves when our investigation was being performed. Admittedly this cone was intended to be employed only for certain purposes, but we consider it necessary to take into account how the cone has been used in practice. The selection of this extreme position in order to elucidate the hazards is justified by Fig. 1, which is reproduced from an article by FROMMHOLD and SCHÜTZ in C. H. F. Müller's brochure for the International Congress of Radiology, Mexico City, 1956 (3). We share DIETHELM's et coll. satisfaction that the short cone is no longer being supplied.

The authors appear to believe that the use of the short cone would disturb our measurements for comparison with those with the long cone. The difference they expect will probably be negligible if the geometric design and centering of the cone are correct.

The observations of DIETHELM et coll. on our discussion about the hazards when working close to the tube housing itself do not deal with the main problem raised by us. In the recommendations of the ICRP, only the permissible dose rate at one meter from the housing is discussed. We consider this recommendation insufficient for such roentgen equipment where it is possible or convenient for the operator to work close to the tube housing in the manner illustrated in Fig. 2, which is reproduced from the paper of DIETHELM et coll. of 1956 (1). They attempt to dismiss our indication with a reference to "Deutsche Normen" (DIN 6811). We must point out, however, that our own suggestion as to what should be added to the ICRP recommendations is indicated in DIN 6812. We cite § 3.16 "Sofern mit besonders ungünstigen Betriebsverhältnissen zu rechnen ist, für die der Strahlenschutz normrechter Röntgeneinrichtungen nicht ausreicht (z. B. keiner Abstand von der Röntgenröhre, . . .) muss durch zusätzliche Massnahmen für ausreichenden Strahlenschutz . . . gesorgt werden". This is exemplified in DIN 6812 § 3.31, and in DIN 6811 § 4.21 "Bei kleinem Abstand von der Röntgenröhre, z. B. der Unterschenkel bei Untertischdurchleuchtung, ist ein Zuschlag erforderlich . . .".

The authors have partly overlooked that our article described the situation as it was in 1956. If our article has caused certain undesirable methods in the use of the image intensifier to be rejected by manufacturers and physicians, we obviously have obtained the desired results of our investigation. That the intensifier plus the roentgen apparatus still has to be considered as roentgen equipment has so far not been questioned by DIETHELM et coll. who appear to agree completely with us as to the correct use of such equipment. We therefore subscribe fully to the conclusion of these authors that only with due observation of general precautions can irradiation of the examiner be kept sufficiently below the 'risk limit'.

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FROM THE PHYSICS DEPARTMENT, CHRISTIE HOSPITAL & HOLT RADIUM INSTITUTE, WITHINGTON, MANCHESTER 20, ENGLAND.

RADIATION HAZARD CONNECTED WITH THE USE OF IMAGE INTENSIFIER FITTED IN CONVENTIONAL ROENTGEN UNITS

Comment by

F. W. TRANTER

I have been rather perturbed, when examining diagnostic units fitted for use with the electronic image intensifier (image amplifier), to observe the lack of attention paid to an obvious radiation hazard.

It concerns (1) the patient, and (2) the radiographer or more frequently the surgeon.

In each instance the hazard arises because the system adopted for viewing the roentgen beam and the beam defining system are not closely related.

Beam viewing is done by an image intensifier with a circular screen. *Beam restriction* is usually done by means of moveable plates giving a rectangular outline to the beam. These plates are positioned by the person viewing through the intensifier eyepiece and, surprisingly, it is necessary to remark that the beam so obtained can never coincide with the screen. The manufacturers may avoid irradiating the head and shoulders of the viewer by providing the usual type of viewing screen with lead glass backing as a surround to the image intensifier; they do not thereby remove the hazard to the patient nor to the hands of the radiologist, further, the screen provided is of little use for viewing by the person using the image intensifier.

Because the field visualised is rather small the most likely method of use is to open the rectangular beam defining apertures until the intensifier is fully illuminated. The edges of the diaphragms are then lost from view and so the roentgen beam could illuminate a much larger area of the patient than is seen, also the hands of the person manipulating the patient could enter the roentgen beam without being seen.

It is not sufficient to fit stops as an answer to this problem so that the edges of the field become tangential to the circle seen through the intensifier since the corners of such a field are still not visualised and may cause damage. It is, however, usually possible to fit a subsidiary circular diaphragm of size just sufficient to cover the screen of the intensifier, and interlocked so that the screening circuits operate only when the diaphragm is in place.

When this has been done the problem of alignment becomes evident. It is necessary that this should be routinely checked by the radiographer in charge of the machine and some means whereby this alignment can be simply adjusted by the radiographer must be provided by the manufacturer.

BOOK REVIEWS

RADIOLOGIC PELVIMETRY. By Ulf Borell and Ingmar Fernström. 97 pages, 49 illustrations and 10 tables. Acta radiol. (1960) Suppl. No. 191. Price: Sw. Kr. 30: —.

Based upon an analysis of about 3 400 roentgenologic pelvimetries pelvic measurements likely to provide information regarding constriction of the inlet and of the distal part of the pelvis are examined. The value of a knowledge of the morphologic appearance of the pelvis is also discussed. After an analysis of the indications for roentgenologic mensuration of the pelvis the authors argue that if these were made stricter fewer pregnant women would be submitted to roentgenologic examination. In another section of the book, the incidence of pelvic constriction is investigated. Constriction of the inlet has become a rare occurrence during the past decade, while constriction of the outlet has not changed, with the result that the latter type now seems to be commoner than the former.

From their results the authors present a new method of making pelvic measurements which provides exact information on the length of the diameters of significance for diagnosis. In working out this method great importance was placed on the roentgen doses, which the authors have been able to reduce considerably.

Autoreview

TRANSVERSALE TOMOGRAPHIE. Von Franz Hammer. 70 Seiten, 73 Abbildungen. Verlag Wilhelm Maudrich. Wien 1959. Price: DM 21. —

This little booklet gives a short account of transverse tomography in theory and practice. The author presents a Transversotome of his own design, the advantages of which are claimed to be simplicity of construction and maintenance, and relatively low price, as compared with other apparatuses of a similar type. A few examples of the diagnostic value of the method, in thoracic and abdominal diseases as well as in those of the skeletal system (cranium and spinal column), are also described. The booklet is easy to read on account of its exemplary brevity and clearness of presentation. The clinical illustrations, on the other hand, are not of particularly good quality, as is often the case with tomographic publications. Neither are the conventional roentgenograms especially good. Owing to the death of the author in 1956 the work was published three years later than had been planned. It therefore contains nothing actually new as several works on the same subject have been published in the meantime.

Stig Fagerberg

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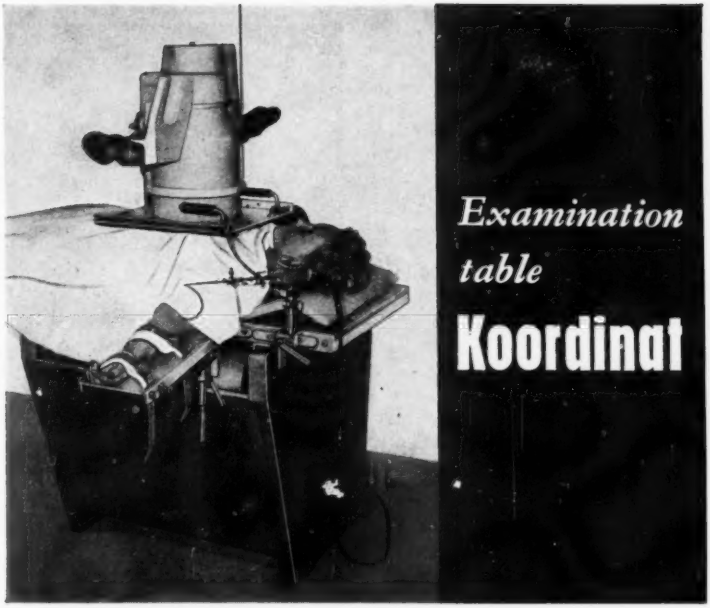

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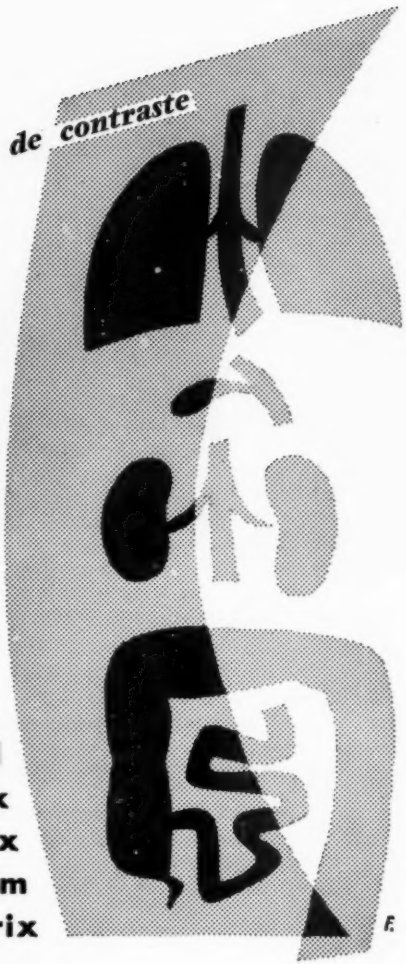

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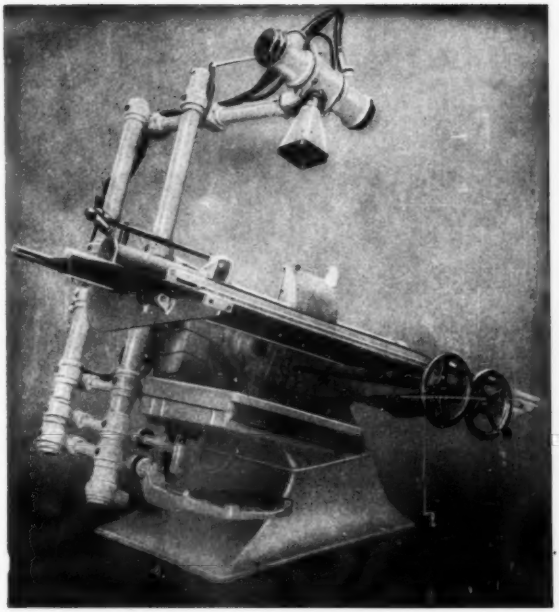

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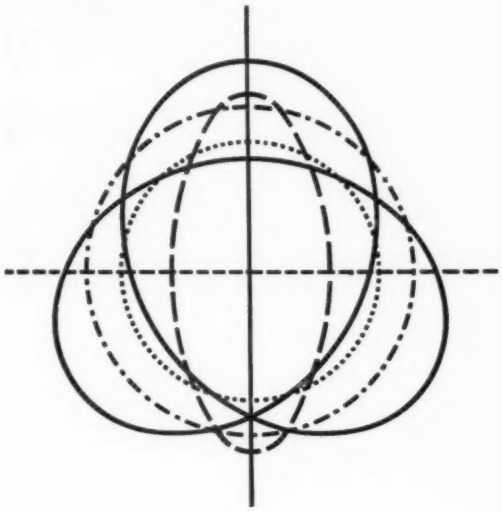

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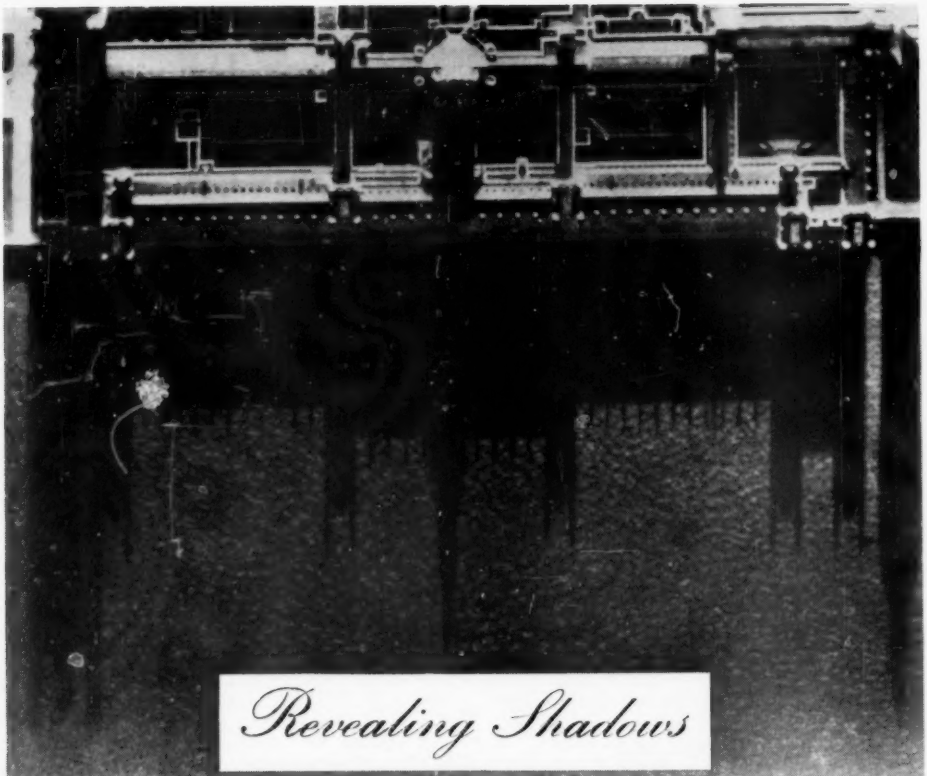

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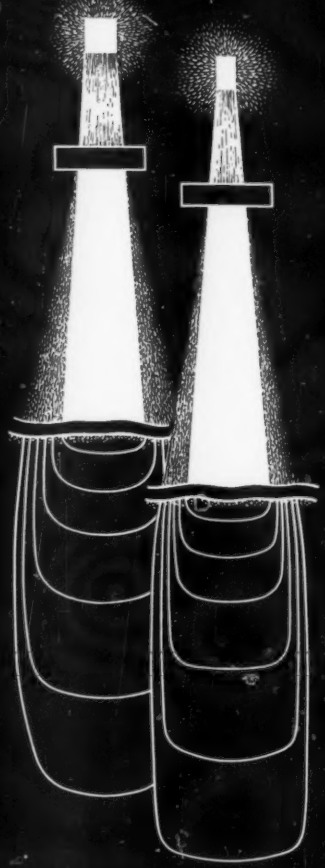

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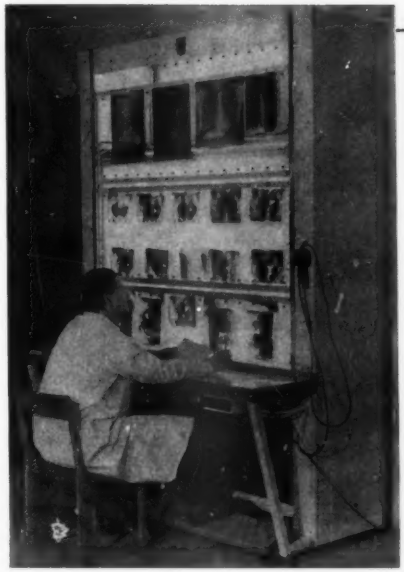

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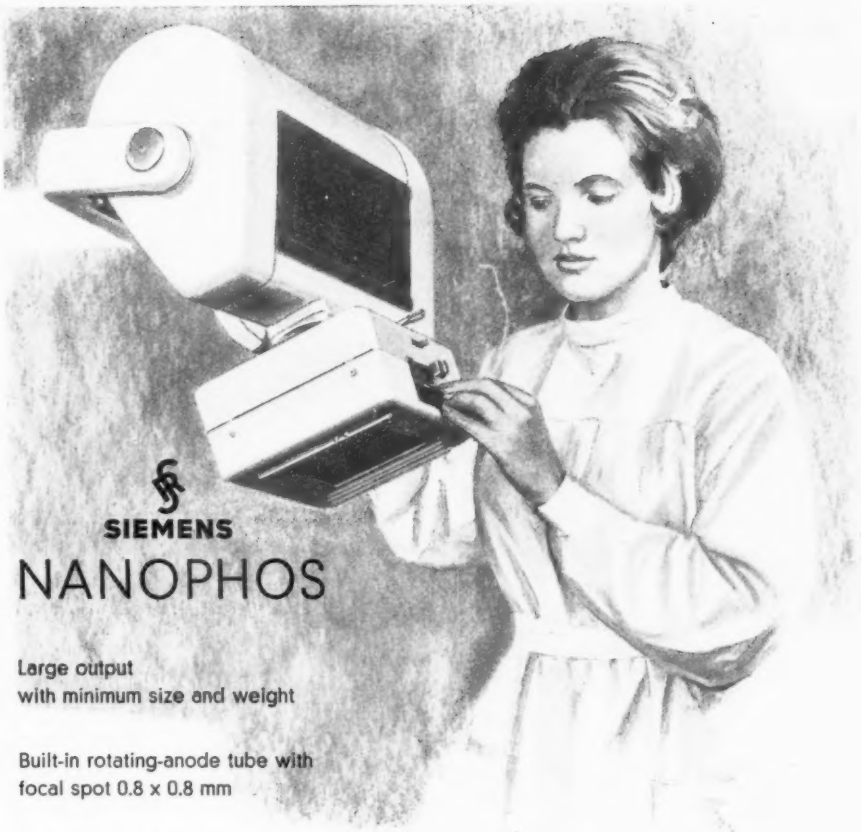


SIEMENS

NANOPHOS

Large output
with minimum size and weight

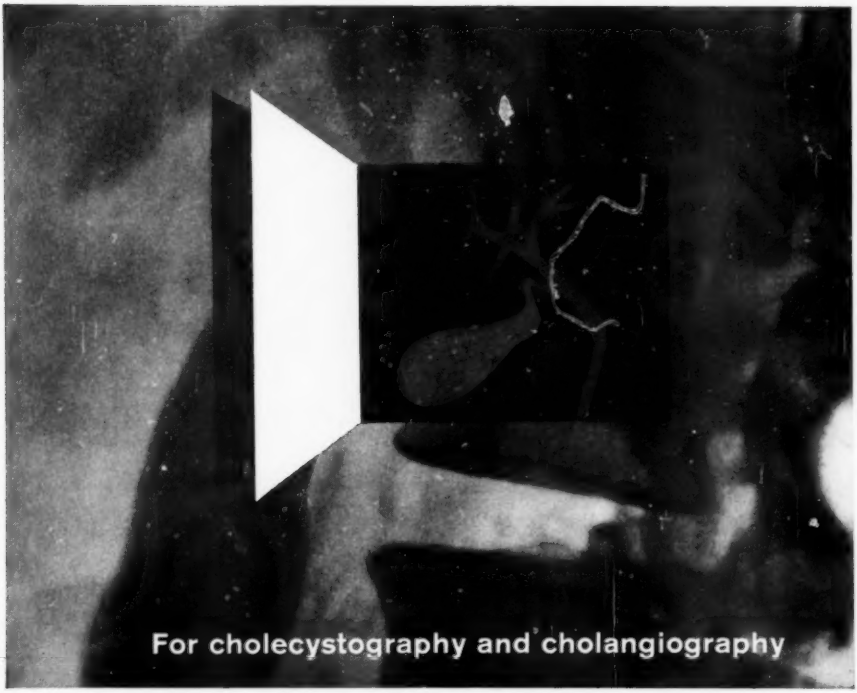
Built-in rotating-anode tube with
focal spot 0.8 x 0.8 mm

Output: 100 mA at 60 kV
70 mA at 100 kV
50 mA at 125 kV

New! **Single-tank x-ray generator with full-wave rectification**

Please request our leaflet

SIEMENS-REINIGER-WERKE AG ERLANGEN · GERMANY



Oral biliary contrast media

Biloptin
new! Solu-Biloptin

Biloptin. Sodium salt of β-(3-dimethylamino-methylenamino-2,4,6-triiodophenyl)-propionic acid.
6 capsules, each of 500 mg.

Solu-Biloptin. Calcium salt of β-(3-dimethyl-amino-methylenamino-2,4,6-triiodophenyl)-propionic acid.
Bottle with 3 g. of active agent in powder form for the preparation of a suspension.

Improved oral radiological diagnosis of the biliary system

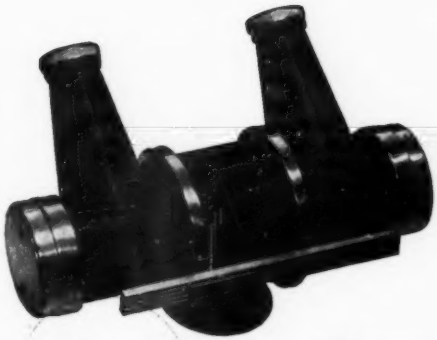
Exceptional tolerance

No disturbing residua of contrast medium in the bowel

Schering

SCHERING A.G. BERLIN/GERMANY

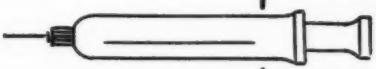
Representatives:
Schering A/S Kopenhagen-Ballerup | Tollef Bredal A/S Oslo | Nordiska A/B Schering Stockholm/Saltsjö-Duvnäs



Machlett Dynamax "150"

An advanced 150 KV rotating anode tube designed for the latest high voltage diagnostic techniques

Modern radiological techniques demand tubes and equipments designed to meet specific requirements. Recognizing this, Machlett Laboratories offers in the Dynamax family the broadest line of rotating anode tubes available today. There is a Dynamax for every diagnostic application.



The Dynamax "150", unique of its kind, is one of many special versions of the Dynamax designed for specific applications; in this case, a number of highly specialized techniques outside the range of so-called standard tubes including cineradiography and millesecond angiocardiography. It extends the useable voltage range up to 150 PKV and provides an unusually high heat storage capacity and heat dissipation rate for extremely rigorous diagnostic service.

Write or wire for full technical data.

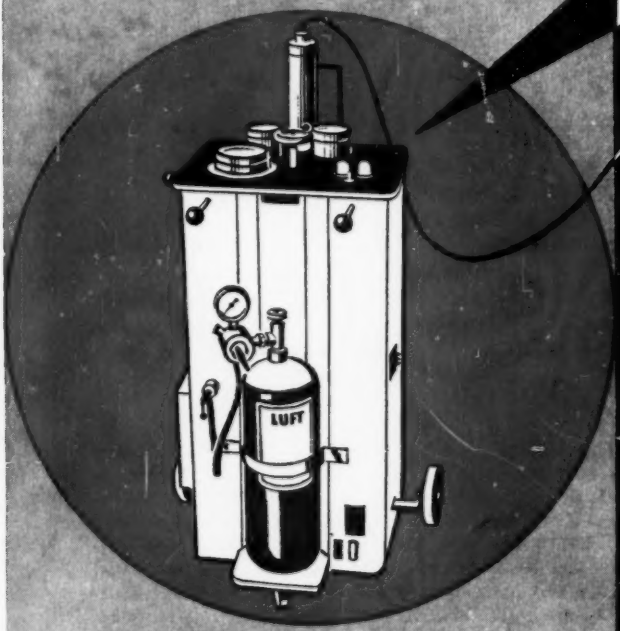
MACHLETT

X-RAY TUBES SINCE 1897 — TODAY THEIR LARGEST MAKER

MACHLETT LABORATORIES, INC.
Springdale, Connecticut

CARDIO-ANGIOGRAPHY

with
Remote Controlled High Pressure
INJECTION SYRINGE
(Gidlund System)



- Variable injection speed
- Remote control of X-ray exposure
- Automatic temperature and pressure control

Ask for special pamphlet

INDUSTRIVÄGEN 23 · STOCKHOLM-SOLNA SWEDEN

ELEMA-SCHÖNANDER

9990

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